SUMMARY STATEMENT

PROGRAM CONTACT: *(Privileged Communication)*
[redacted]
[redacted]

Release Date: 03/10/2026
Revised Date:

Application Number: 1R43GM136218-01

Principal Investigators (Listed Alphabetically):
[redacted] (Contact)

Applicant Organization: [redacted]

Review Group: ZRG1 BCMB-A (22)
Center for Scientific Review Special Emphasis Panel
Small Business: Biochemistry, Cellular and Molecular Biology

Meeting Date: 02/12/2026
Council: MAR 2026
Requested Start: 09/01/2026

Opportunity Number: PA-24-246
PCC: GMS -SO

Project Title: Machine Learning Platform for Accelerated Discovery of Novel Kinase Inhibitors Targeting Treatment-Resistant Solid Tumors

SRG Action: Impact Score:55
Next Steps: Visit https://grants.nih.gov/grants/next_steps.htm
Human Subjects: 10-No human subjects involved
Animal Subjects: 30-Vertebrate animals involved - no ass. conditions noted
Participant Sex:
Participant Race and Ethnicity:
Participant Age:
0-No human subjects

Project Year	Direct Costs Requested	Estimated Total Cost
1	225,000	279,000
TOTAL	**225,000**	**279,000**

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

1R43GM136218-01 [redacted]

RESUME AND SUMMARY OF DISCUSSION: The application was not discussed. Written critiques from the assigned reviewers are provided below.

DESCRIPTION (provided by applicant): This Phase I SBIR application proposes to develop a machine learning platform for discovery of novel kinase inhibitors targeting treatment-resistant solid tumors. The platform combines graph neural networks for molecular property prediction with a generative chemistry module for de novo compound design. Phase I will validate the platform by generating and experimentally testing 50 novel compounds against a panel of kinase targets implicated in treatment resistance, with success defined as identification of at least 3 compounds with IC50 values below 100 nM. The company has developed a proprietary training dataset of 2.3 million kinase-ligand interaction pairs curated from public and proprietary sources.

PUBLIC HEALTH RELEVANCE: Treatment resistance remains a primary cause of mortality in solid tumor malignancies. Novel kinase inhibitors targeting resistance mechanisms could improve outcomes for patients who have exhausted standard therapies. AI-driven drug discovery could accelerate identification of effective compounds and reduce development costs.

CRITIQUE 1

Significance: 3

Investigator(s): 6

Innovation: 5

Approach: 7

Environment: 5

Overall Impact: This application proposes an ML-based drug discovery platform for kinase inhibitors. While the general area of AI drug discovery is active, this application does not convincingly demonstrate what is novel about this specific platform compared to numerous existing commercial and academic approaches. The preliminary data are limited to in silico validation with no experimental confirmation. The PI has a computational background but no experience in medicinal chemistry or drug development. The approach lacks essential components including ADMET prediction, selectivity profiling, and a clear lead optimization strategy. Multiple significant weaknesses dampened enthusiasm considerably.

1. Significance:

Strengths

- Kinase inhibitor resistance is a clinically important problem.
- Accelerating drug discovery timelines is a worthwhile goal.

Weaknesses

- The specific kinase targets are not clearly defined. "Kinases implicated in treatment resistance" is too broad to constitute a focused drug discovery program.
- The application does not articulate why existing kinase inhibitors fail or what structural features of novel compounds would overcome resistance.

2. Investigator(s):

Strengths

- The PI has expertise in machine learning and graph neural networks.

Weaknesses

- The PI has no background in medicinal chemistry, pharmacology, or drug development. These are essential disciplines for translating computational predictions to viable drug candidates.
- No medicinal chemist or pharmacologist is on the team. This is a critical gap.
- The PI has no prior SBIR/STTR funding and no publications in drug discovery.
- No advisory board with drug development expertise is described.

3. Innovation:

Strengths

- The use of graph neural networks for molecular property prediction is technically sound.

Weaknesses

- Multiple commercial platforms (Schrödinger, Atomwise, Recursion, Insilico Medicine) already offer AI-driven kinase inhibitor discovery. The application does not differentiate this platform from these established competitors.
- The generative chemistry module is described at a high level without sufficient technical detail to evaluate novelty.
- The training dataset of 2.3 million interactions, while large, appears to be primarily derived from public databases (ChEMBL, BindingDB). The proprietary component is not described.

4. Approach:

Strengths

- The proposed experimental validation of 50 compounds is a reasonable approach to platform validation.

Weaknesses

- No ADMET (absorption, distribution, metabolism, excretion, toxicity) prediction is incorporated into the platform. Generating potent compounds that are not drug-like is a well-known failure mode in computational drug discovery.
- The success criterion of 3 compounds with IC50 below 100 nM does not address selectivity. Non-selective kinase inhibitors are a major source of toxicity.
- The experimental validation plan describes cell-free kinase assays only, with no cell-based assays to confirm cellular activity.
- No lead optimization strategy is described. Hit identification without optimization is insufficient for a drug discovery program.
- The chemistry synthesis plan for 50 compounds is not described. Who will synthesize these compounds? What is the timeline and cost?
- The computational validation results presented (AUROC of 0.89 on held-out test set) are not compared against baseline models or existing platforms, making them impossible to evaluate.

5. Environment:

Strengths

- Adequate computational infrastructure.

Weaknesses

- No wet lab capability is described. All experimental work depends on external CROs that are not identified.
- No letters of support from synthesis or screening partners.

Vertebrate Animals:

Not applicable for Phase I.

Budget and Period of Support:

The budget includes $85,000 for compound synthesis and screening at external CROs that are not identified. This should be clarified if funded.

CRITIQUE 2

Significance: 4

Investigator(s): 7

Innovation: 6

Approach: 8

Environment: 6

Overall Impact: The application proposes an ML platform for kinase inhibitor discovery. The concept is not novel and the application has numerous fundamental weaknesses. The team lacks essential drug development expertise, the approach is missing critical components, and the preliminary data are entirely computational. This application is not competitive in its current form and would require major restructuring to address the identified concerns.

1. Significance:

Strengths

- Drug resistance in solid tumors is clinically important.

Weaknesses

- The target kinases are not specified with sufficient precision to evaluate significance.
- No clear rationale for why computational discovery will succeed where conventional approaches have not.

2. Investigator(s):

Weaknesses

- The single PI lacks any drug development experience. This is a drug discovery proposal led by someone who has never discovered a drug.
- No co-investigators or consultants with medicinal chemistry expertise.
- No clinical or pharmacology input into target selection.

3. Innovation:

Weaknesses

- Graph neural networks for molecular property prediction are widely used. No novel methodological contribution is described.
- The platform is essentially a combination of existing techniques without clear differentiation.

4. Approach:

Weaknesses

- No ADMET prediction, no selectivity profiling, no lead optimization, no cell-based validation.
- The synthesis and screening plan is not developed. External partners are not identified.
- Success metrics do not address drug-likeness or selectivity.
- In silico-only preliminary data are insufficient.

5. Environment:

Weaknesses

- No wet lab facilities. Complete dependence on unidentified external partners.

Budget and Period of Support:

Recommend as Requested

CRITIQUE 3

Significance: 3

Investigator(s): 5

Innovation: 5

Approach: 6

Environment: 4

Overall Impact: While AI-driven drug discovery is a promising field, this application does not make a convincing case for the novelty or feasibility of this specific platform. Fundamental gaps in team expertise, approach design, and experimental infrastructure prevent recommendation for funding at this time.

1. Significance:

Strengths

- Important clinical area with unmet need.

Weaknesses

- Vague target definition undermines the significance argument.

2. Investigator(s):

Strengths

- ML expertise is relevant to the computational component.

Weaknesses

- The absence of drug development expertise on the team is a fundamental weakness that cannot be addressed by computational skill alone.

3. Innovation:

Strengths

- The general approach of combining generative chemistry with predictive modeling has promise.

Weaknesses

- Not sufficiently differentiated from existing commercial platforms.

4. Approach:

Strengths

- Experimental validation is proposed rather than purely computational.

Weaknesses

- Multiple essential drug discovery components are missing.
- The experimental plan is underdeveloped.

5. Environment:

Strengths

- Computational resources are adequate.

Weaknesses

- No experimental infrastructure or formalized external partnerships.

Budget and Period of Support:

Recommend as Requested

THE FOLLOWING SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE, OR REVIEWERS' WRITTEN CRITIQUES, ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS: ACCEPTABLE.

PARTICIPANT SEX CODE: ACCEPTABLE

PARTICIPANT RACE AND ETHNICITY CODE: ACCEPTABLE

PARTICIPANT AGE CODE: ACCEPTABLE

COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

Footnotes for 1R43GM136218-01; PI Name: ■■■■■■■■■■■■
NIH has modified its policy regarding the receipt of resubmissions (amended applications). See Guide Notice NOT-OD-18-197 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-197.html. The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. Some applications also receive a percentile ranking. For details on the review process, see http://grants.nih.gov/grants/peer_review_process.htm#scoring.

MEETING ROSTER

Center for Scientific Review Special Emphasis Panel

CENTER FOR SCIENTIFIC REVIEW

Small Business: Biochemistry, Cellular and Molecular Biology

ZRG1 BCMB-A (22)

02/12/2026

Notice of NIH Policy to All Applicants: Meeting rosters are provided for information purposes only. Applicant investigators and institutional officials must not communicate directly with study section members about an application before or after the review. Failure to observe this policy will create a serious breach of integrity in the peer review process, and may lead to actions outlined in NOT-OD-22-044 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-22-044.html, including removal of the application from immediate review.

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Consultants are required to absent themselves from the room during the review of any application if their presence would constitute or appear to constitute a conflict of interest.