Dear Hiring Manager,

I am writing to express my sincere interest in joining \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. I believe my background in computer-aided drug design and protein engineering makes me a strong candidate for this role.

In my current role at GeneCentrix as a research scientist, I am primarily responsible for *de novo* generative molecular design within a pharmaceutical co-development program with AbbVie. The goal of the initiative is to develop a peptide ligand that selectively binds to a cell-surface biomarker specific to target tissue. This targeting moiety can be envisioned as a fused element to existing biologics for focusing the activity of these biologics to specific tissues, thereby eliciting novel or safer therapeutic effects.

The work has engaged several key algorithms and concepts that overlap between protein engineering and computer-aided design of small molecule drugs: namely conformational search, energy calculation, stability analysis, analysis and mapping of non-covalent ligand-receptor interactions and critical analysis and definition of features (e.g. pockets) of 3D structural models, be they generated from crystallography, cryo-EM, AI structure prediction or homology modeling. More, specifically, I have used computational molecular docking, B-factor analysis, cross-species sequence alignment, and molecular surface analysis to identify pockets where the structure was reliable and highly conserved. Many of the workflows involved large numbers of molecular entities, requiring me to generate high throughput python-based scripts, including one to supervise a docking screen of randomized amino acid peptides for lead generation. The docking screen I implemented generated preferred conformations and energy scores for thousands of randomly mutated peptides, which were then analyzed statistically based on energy scores and residue contact area. Once hit peptide candidates were identified, I worked on optimizing these hits by extending the peptides in length one amino acid at a time to the C- or N-termini, to identify amino acids that capture potent, new noncovalent interactions, with an emphasis on creating salt bridges and hydrophobic interactions including cation-pi, anion-pi, and pi-stacking interactions. In the course of this work, I was introduced to new developments in the field, including the recent paper by Cao et al from the laboratory of Dr. David Baker, which was pursuing a similar platform to ours. I worked on capturing insights from this orthogonal effort to improve our designs, learning in the process how to take advantage of useful advances in the published or patent literature in *de novo* generative molecular design. I was able to achieve the deliverable of this project and sent 4 *de novo* generative molecular designs to our pharmaceutical partner AbbVie for validation.

While *de novo* generative molecular design has been my focal point at GeneCentrix, I have also had the opportunity to work on projects with the data science and software engineering teams. Most notably I have invested significant effort towards implementing a machine learning model designed to predict drug target affinity, into our drug profiling software. The model draws on deep learning strategies for feature vector extraction from drug SMILES and protein sequences, graph mining of known affinity values between drugs and proteins, and regression based predictive measures.

I believe my experience at GeneCentrix, my graduate studies at NYU in computer aided drug and biologics design, and my passion for drug discovery make me a unique yet strong candidate to be an effective \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. What I believe sets me apart from other candidates is my passion, creativity, and drive to succeed. I invest a great deal into my professional development outside of work hours. I have always believed that as my skillset grows, it expands my ability to make an impact in driving the advancement of innovative therapeutics. I am dedicated to pursuing this fascinating cross disciplinary field at the intersection of biology, physical biochemistry, and artificial intelligence because I genuinely believe it will have a transcendental effect on therapeutics and reshape the way we handle healthcare—positively affecting the quality and standard of care for patients.

Thank you for your time and consideration,

Sincerely,

Nicholas Woytowitz