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Dear Guests of the American Cancer Society CEOs Against Cancer,

I am writing to reflect upon the past year of funding from my American Cancer Society Research Scholar Grant. I thank you again for your generous support of my work, without which none of my discoveries would be possible. My research focuses upon molecularly-targeted therapeutics, or "personalized medicine." It studies specific features present in individual patients' leukemia cells that predict response to specific medications and thus guide individualized treatment choice. Because personalized leukemia treatments act on features specific to leukemia, but not normal cells, targeted drugs can generate dramatic improvements in response, survival, and even cure rates--often with minimal and/or very tolerable side effects. Thus, my research seeks to identify ways to make future cancer treatments both more effective *and* less toxic.

The particular disease I have been funded to study is called Ph-like acute lymphoblastic leukemia (ALL). It is phenomenal that current chemotherapy cures the vast majority of children with ALL. However, not all children are cured with our best approaches. When we look at why this happens, we often find that these children have Ph-like ALL. The disease is called Ph-like because it shares features with the subtype Ph+ ALL (named for its discovery in Philadelphia). The most important shared feature between Ph+ and Ph-like ALL is the presence of abnormalities in the leukemia cells' DNA (mutations) that abnormally activate specific enzymes called kinases. Activated kinases promote rapid cancer cell growth, but this effect can be blocked by kinase inhibitors. Indeed, kinase inhibitors can kill cancer cells with these mutations while sparing non-cancerous cells, making them attractive treatment options. Kinase inhibition is currently standard therapy for Ph+ ALL, but not yet Ph-like ALL. In part, this is because Ph-like ALL is notoriously harder to diagnose and has not been as extensively studied. For these reasons I proposed this grant.

I am pleased to say we are making progress addressing all major questions proposed in the grant application. Our data show that approximately 20% of adults with ALL have Ph-like disease, making this the second most common subtype of adult ALL. Indeed, in adults over age 40, nearly 2/3 of ALL patients have either Ph-like or the highly analagous Ph+ subtype, meaning kinase inhibition potentially could benefit the majority of adult ALL. This observation highlights the importance of understanding disease biology to optimize treatment. Although many different mutations can occur in Ph-like ALL, we found that mutations in one particular gene (called CRLF2) were present in ¾ of our adult Ph-like ALL cases and that CRLF2+ cases could be easily detected by a rapid test developed for this grant. Although our diagnostic assay is quite robust for detecting CRLF2+ Ph-like ALL cases, we also noted some limitations that mean it could fail to detect other Ph-like patients who would likely benefit from targeted therapy; we are continuing to refine our test and compare it to existing and emerging diagnostic methods. Finally, we have recently begun long-term experiments that test combinations of relatively low toxicity chemotherapy plus medications that inhibit kinases. These will take many months for the data to be interpretable and I look forward to updating you on their progress in due time. Importantly, these results will then guide the design of future clinical trials, studies we plan to initiate once the data are mature.

The American Cancer Society continues to play a crucial role in my scientific and professional success; it has helped me continue to focus upon the mission of improving cures and optimizing therapy for people affected by leukemia. I am greatly indebted to the Society and all the hard work that goes into supporting cancer research and patients alike. I thank you for your ongoing support and your hard work for the cause.

Sincerely,

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Grantee: American Cancer Society Research Scholar

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