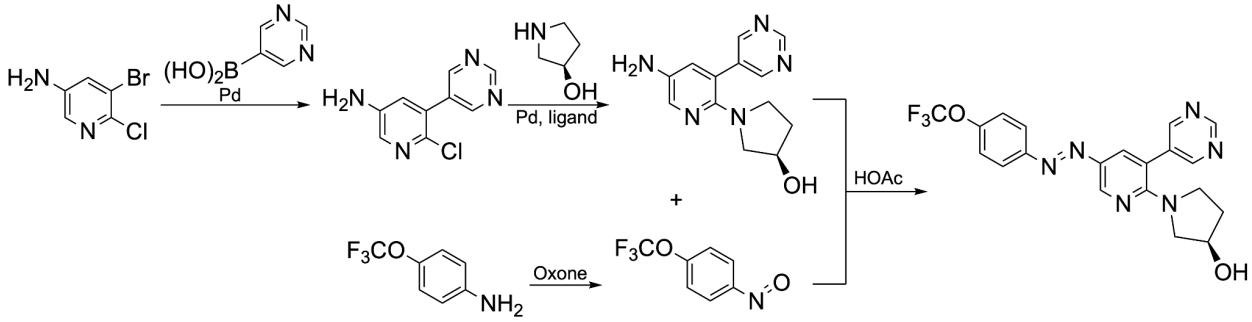
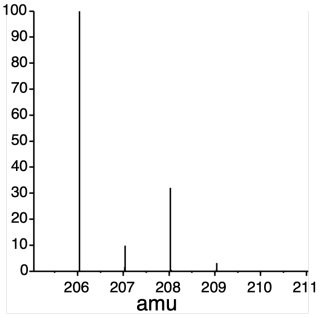
The goal of this project was to create a version of the current cancer drug Asciminib that can be activated with light. Light can be used to selectively activate drugs at the location of disease, which decreases the potential for side effects and risks. I was trying to create an azo-asciminib which means my compound would have a nitrogen nitrogen double bond which allows the drug to flip conformations, cis to trans in order to selectively activate my drug under certain wavelengths of light.

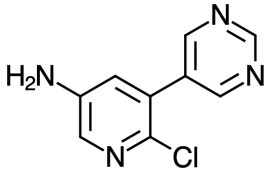
Chronic myeloid leukemia is a cancer due to a chromosome 9 and 22 translocation, resulting in the Philadelphia chromosome. This fusion leads to an oncogene, BCR-ABL, which creates an abnormal protein with a ABL1 kinase domain, permanently activating the protein. The BCR-ABL protein functions as a tyrosine kinase and disrupts normal cell growth regulation by excessively signaling cell division. Asciminib is the latest generation of drug that has been synthesized to inhibit this kinase. What makes it unique is that it is the first approved allosteric inhibitor of the dysfunctional enzyme. This means that the drug binds to the enzyme in places other than the active site, which is where the enzyme performs its chemical reactions and is the classic site of inhibition. Because Asciminib works in a complementary fashion to other drugs, it can be used in concert with those drugs as part of a cancer drug cocktail. Having cocktails of drugs with different modes of action helps limit the potential of the target enzyme to mutate and grow resistant to therapies. In my synthesis below of trying to create an azo-asciminib I have only been able to complete the first step successfully. The second step is very tricky and between previous worker of this project Tess Anthony and I we have tried about 6 different reactions to run in this step and so far nothing has worked. At the end of my time this summer we got a lot closer to figuring out a reaction that might make the second step product we want but I didn't have enough of that product to test and make sure it was correct. So I'm predicting that we have found the reaction that will work. I'll just need more time to finish and run this reaction. Once I get this second step to work we predict I will be able to complete my final compound of my drug.

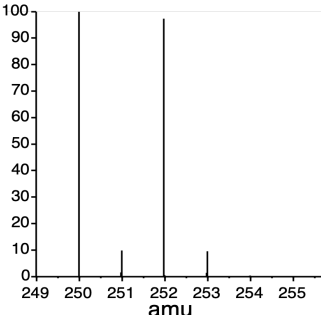


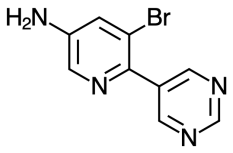
Seeing that the second step wasn't working we went back to the first step product to make sure it was even the correct molecule we wanted. During reactions many different products can be created based on what reacts with what. So we ran a GC mass spec on my first step product to prove that it was what we predicted it to be. So below on the left we can see the two possible products I could have created, and knowing that each compound would have different masses because Cl and Br have different mass numbers on the periodic table lets us use the picture on the right to determine which compound matches best. So for my product the predicted mass was 206 and using the picture on the right we find that at the biggest peak on top and by zooming in below that we see the different peaks and these peaks best match the peaks of the

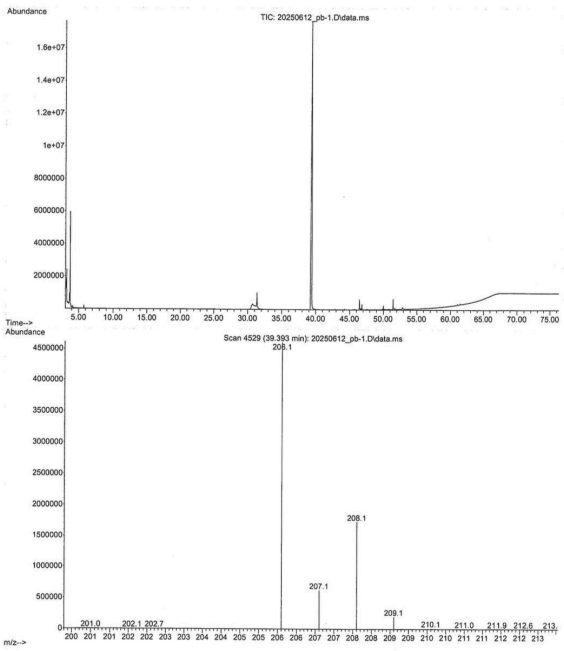
top left compound which has the Cl which is what we predicted originally and wanted my product to be. So this instrument helps us prove that my first step product was indeed what we wanted it to be and allows us to further work on my synthesis.











This product is important to me and the outside world because chronic myeloid leukemia is a very common type of cancer and people are fighting every day to get better from this disease. So with my work in trying to reduce the side effects of an already proven working drug for this cancer it should help people feel better and not get as sick. Which would ultimately start a trend for creating more drugs like this. So far an azo version of asciminib has not been created yet so for me and Albion College it would allow us to write a paper and publish my work to share all over the world. My future plans are to continue working on this project during my senior year at Albion College to try and finish this drug. Also I plan on presenting at Elkin Isaac in the spring to share my work with my classmates and faculty. This work was my first time doing research so it taught me so much and gave me a great experience. I learned how to stay consistent in work even when things weren't reacting how they should and made it hard. On the flip side of this though it pushed me to want to work harder to complete my drug and seeing others in my lab succeed pushed me further. Thank you FURSCA for allowing me this opportunity to learn and grow in the workforce and as a person.