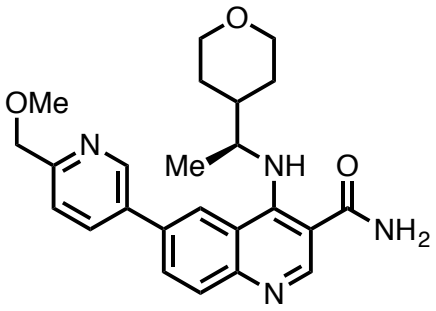
Engle Lab Group Meeting
July 21, 2016

Team Challenge #6
Presenter: Keary Engle

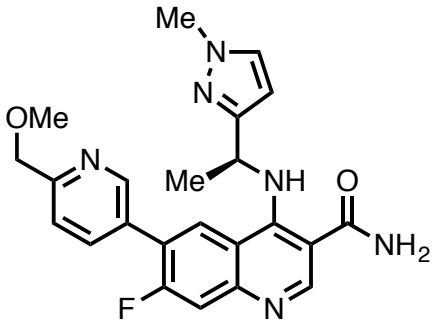
DNA double-strand breaks are a form of DNA damage that can be induced by radiation or chemical exposure. The ataxia mutated (ATM) kinase detects DNA double-strand breaks and signals for activation of downstream DNA repair machinery. Inhibition of ATM in conjunction with clically induced DNA damage in cancer tumor cells is thus a promising approach to cancer treatment.

AstraZeneca recently published a series of selective and potent ATM inhibitors bearing a quinoline 3-carboxamide core structure, including **AZ-1** and **AZ-2**, that also possess ADME properties that allow for oral administration.

For this Team Challenge, you are part of a medicinal chemistry team focused on the synthesis of this series of compounds. Working with your team, propose a modular retrosynthetic strategy to access **AZ-1** and **AZ-2**. Using that strategy, for each of two compounds below, propose forward syntheses that are *concise, stereoselective.* You are not permited to use a computer for this Team Challenge but may ask Keary regarding commercial availability of starting materials.



AZ-1



AZ-2

Degorce, S. L. *et al.*, *J. Med. Chem.* **2016**, *59*, 6281–6292.