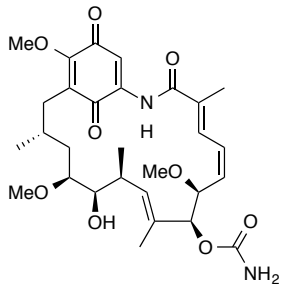
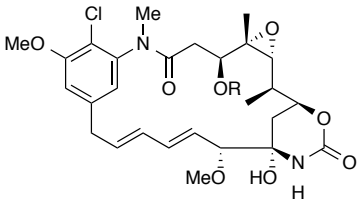
Workshop 3

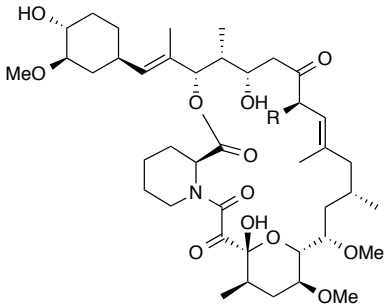
1. Consider the three following bacterial polyketides.



Geldanamycin
Streptomyces hygroscopicus var. *geldanus*
Antitumor



Ansamitocin P3
R = $COCHMe_2$
Actinosynnema pretiosum
Antitumor



FK506
R = CH_2-CH=CH_2
Streptomyces hygroscopicus var. *hygroscopicus*
Immunosuppressant

a. Redraw each compound and show its head and tail.

b. For each compound state:
   (i) how many modules you would expect in its biosynthetic protein(s) (include a starter unit loading module);
   (ii) Which extender units would be used by each module;
   (iii) Which modifying domains would you expect to be present in each module?

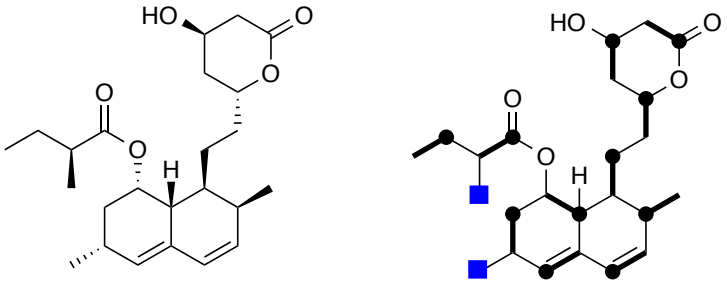
c. For each compound, what would the starter unit have to be?

d. For each compound, what would the likely tailoring steps be?

e. What are the similarities between the 3 biosynthetic pathways?

f. Suggest some potential engineering experiments.

2. Consider the biosynthesis of Lovastsin by the fungus *Aspergiullus terreus*.



a. Draw out all the intermediates during the biosynthesis of lovastatin nonaketide.

b. What must be the tailoring steps ?

b. How could the biosynthesis of lovastatin be engineered?