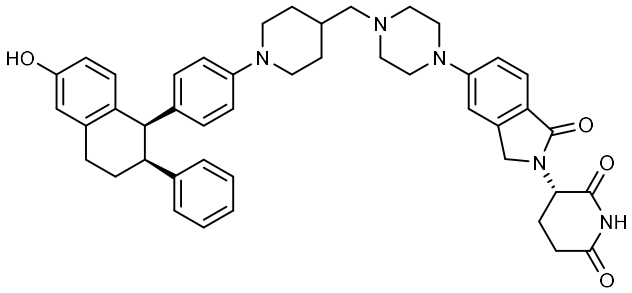
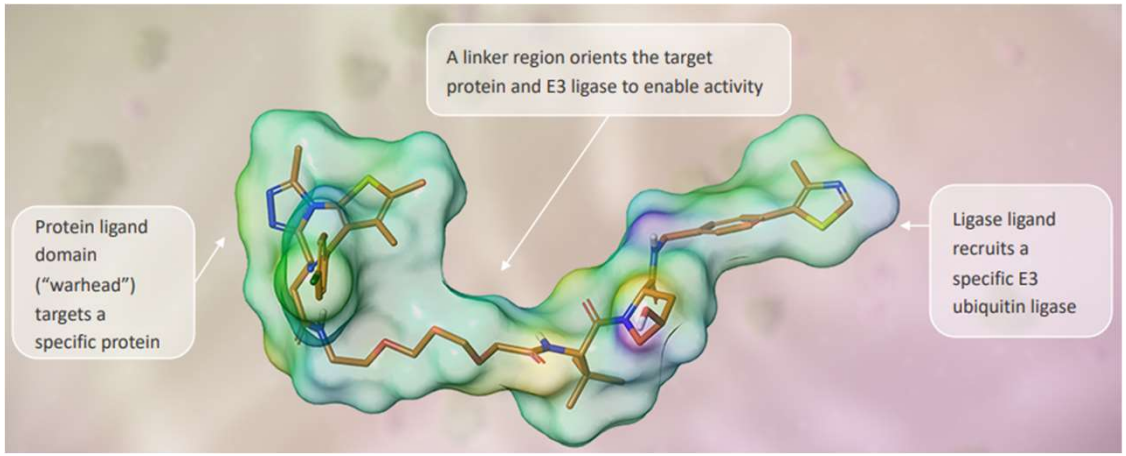
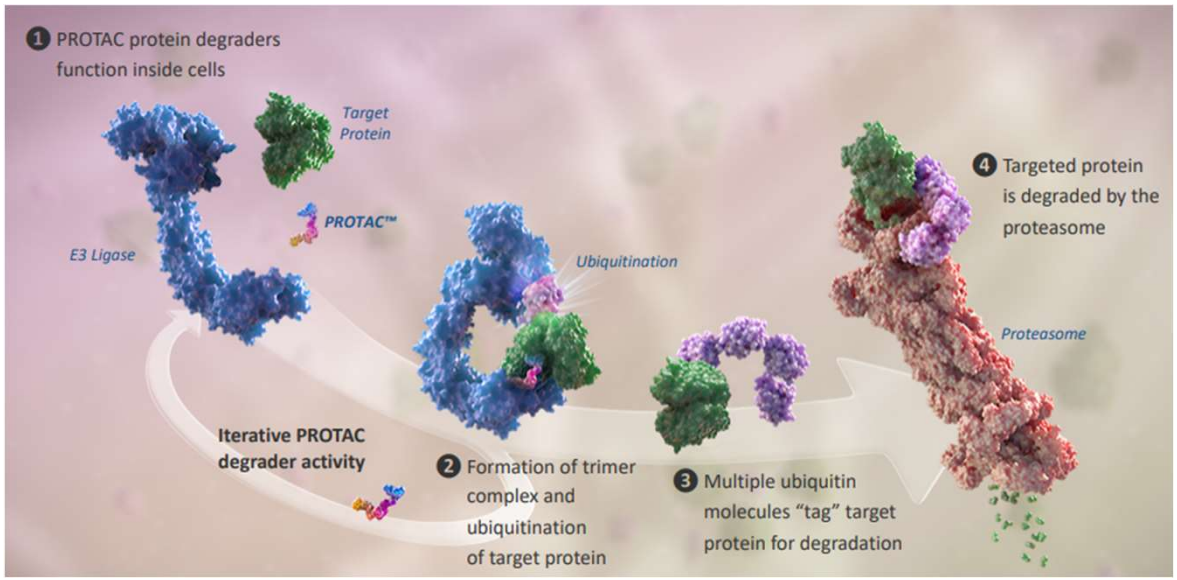
ARV-471

ARVINAS



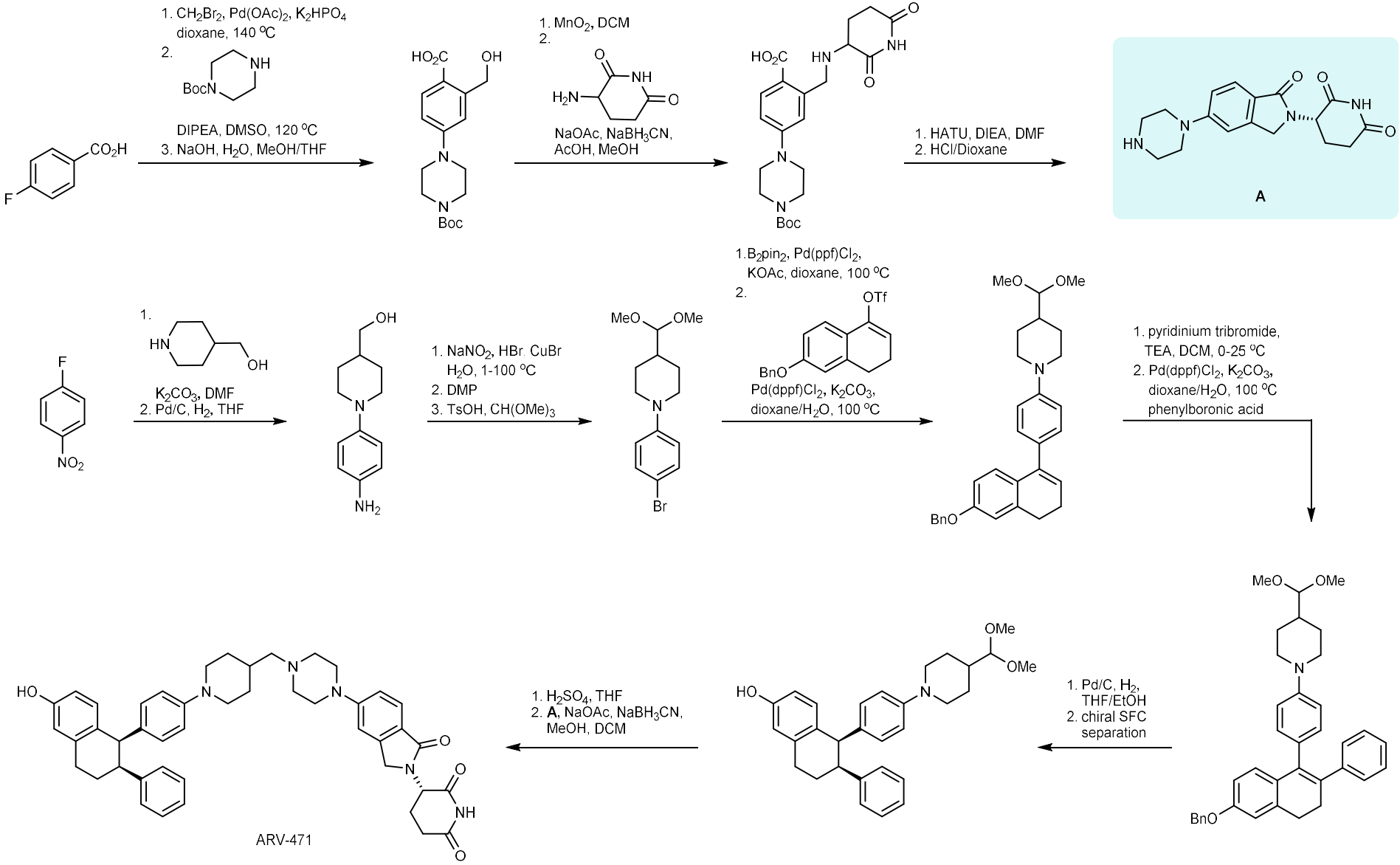


- First PROTACs (proteolysis-targeting chimeras) to enter clinical trials (along with ARV-110)
  - PROTAC: chimeric, modular small molecule engineered to induce degradation of disease-causing proteins by the ubiquitin-proteasome system
  - Potential advantages:
    - Overcome target protein overexpression
    - Selectively eliminate mutated proteins
    - Use of allosteric sites to degrade undruggable targets
- Currently in Phase II trials for breast cancer
- Can be taken orally
- Targets estrogen receptor and binds cereblon (functions as substrate receptor of E3 ubiquitin ligase complex)
  - Short, rigid, nitrogen-containing linker were best for the androgen and estrogen receptors



https://ir.arvinas.com/static-files/e04cc75d-eaf0-4b83-8b7a-68537fe79dc8 . https://cen.acs.org/pharmaceuticals/drug-discovery/Arvinas-unveils-PROTAC-structures/99/i14

Patent Route:



US20180228907A1