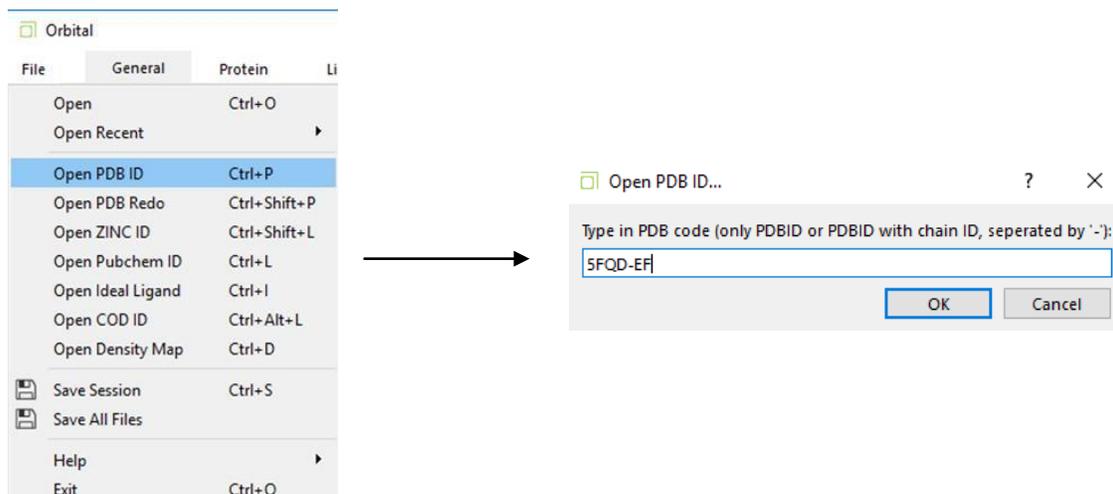
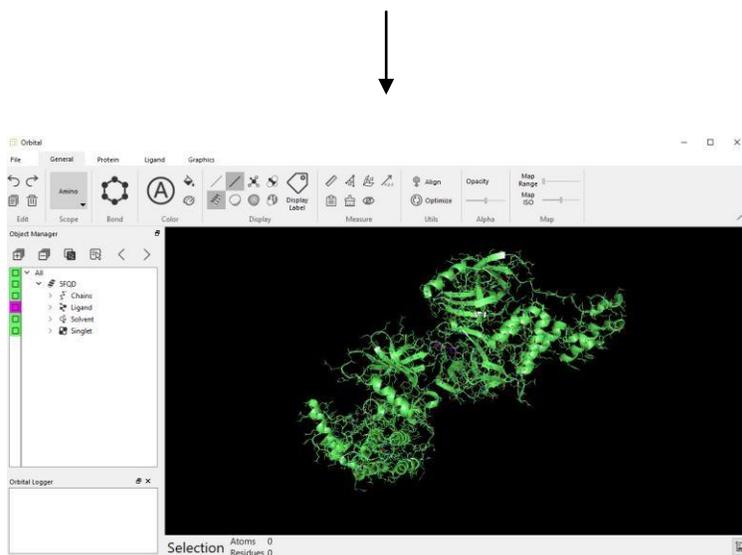
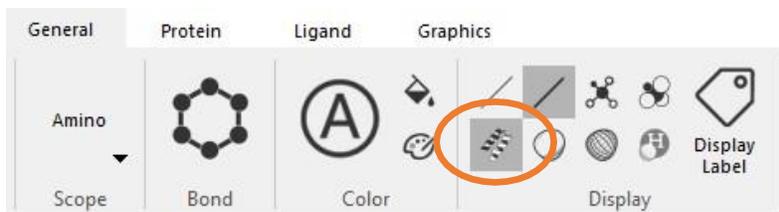


# Ubiquitin E3 ligase targeting drug - revlimid

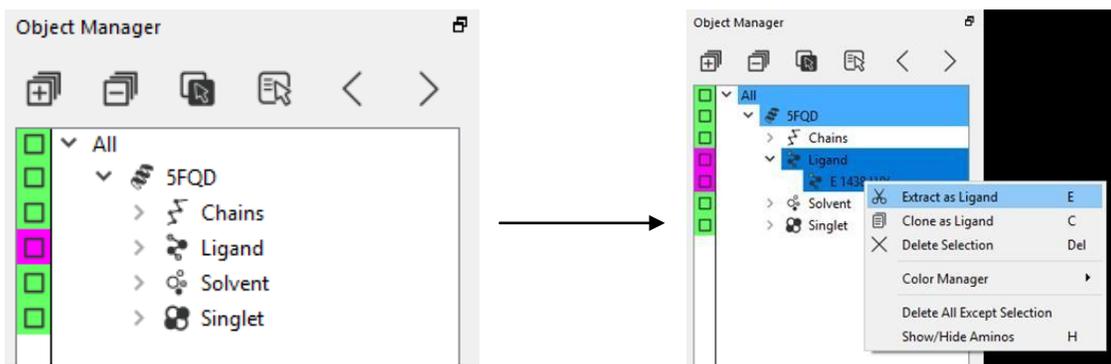
1. **Open** Orbital from the desktop. In the **File** dropdown menu, select **Open PDB ID** (Ctrl+P).
2. In the **Open PDB ID** popup window, enter the PDB ID 5FQD-EF and select **OK** in order to open the CRL4<sup>CRBN</sup> ubiquitin ligase in complex with lenalidomide.



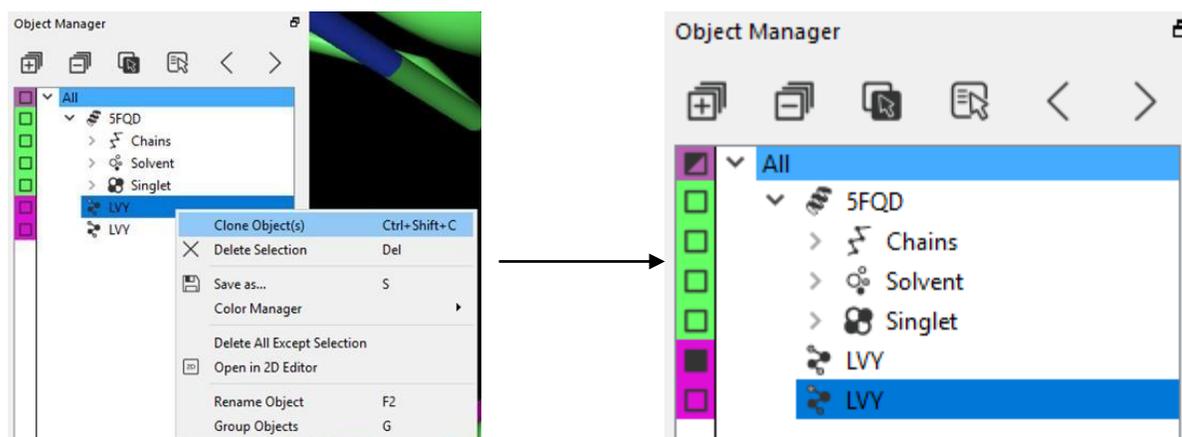
3. Under the **General** tab select the **Cartoon** setting in the **Display** panel in order show the protein in its cartoon structure.



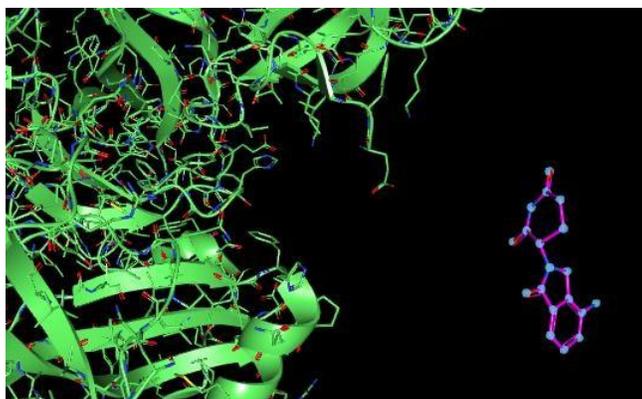
- Next, open the dropdown menu for 5FQD in the **Object Manager** by selecting the downward facing caret next to the name.
- Select the ligand tab and right click **E1438 LVY** and select **Extract Ligand (E)**. (note: always dock a ligand into an un-occupied pocket )



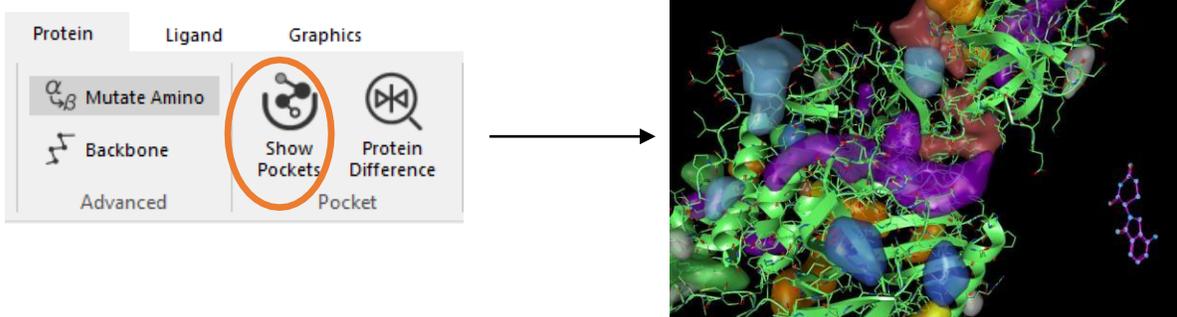
- Right-click on LVY and select **Clone Object**. Deselect the original ligand and select the clone. Next, click the highlighted box to the left of the object.



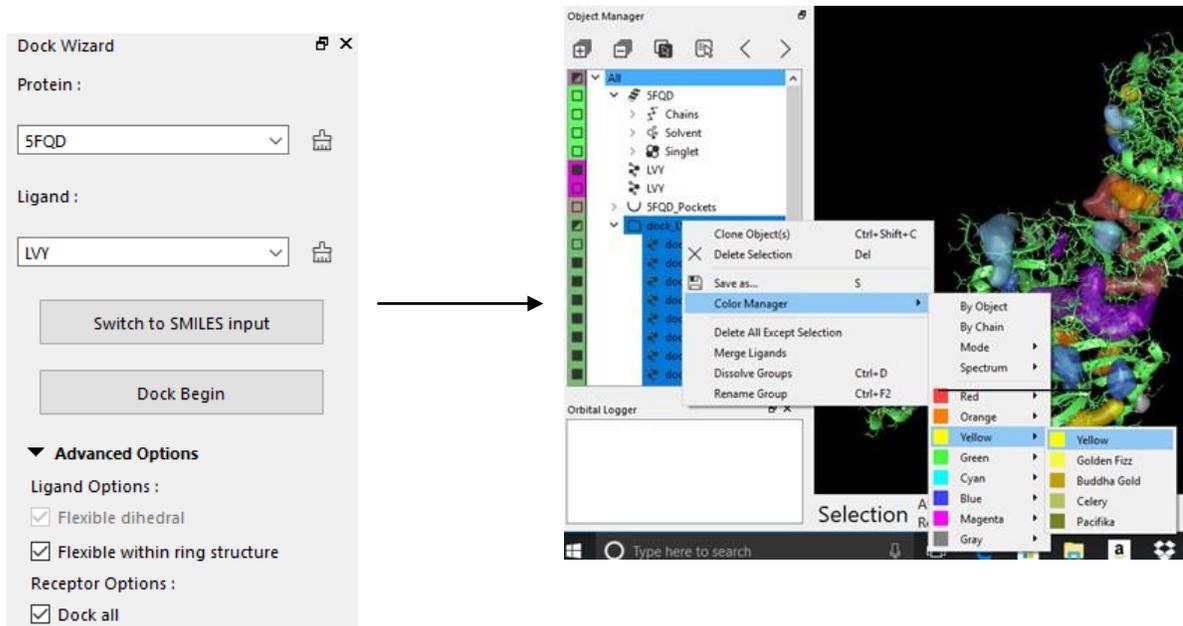
- In order to zoom in on the ligand click the name in the Object Manager with the scroll button on the mouse. Select the ligand while holding **Ctrl + Scroll** button on the mouse to move the ligand away from the protein.



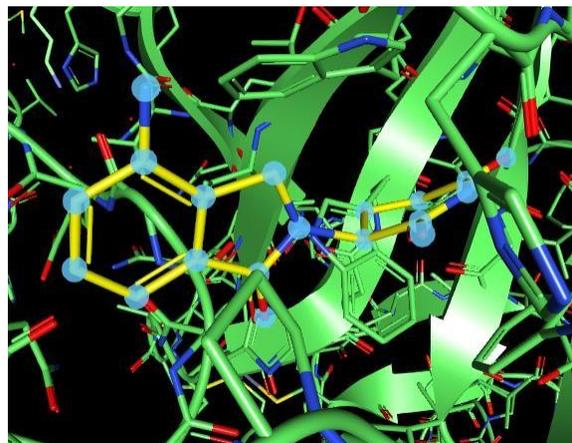
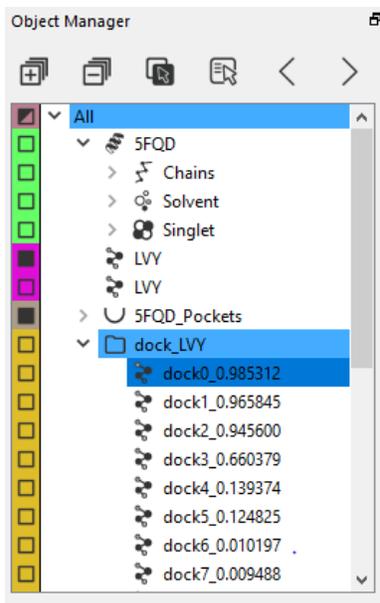
- In the **Protein** tab select **Show Pockets** under the **Pocket** panel (circled in orange below). Orbital will then assign pockets to the protein surface.



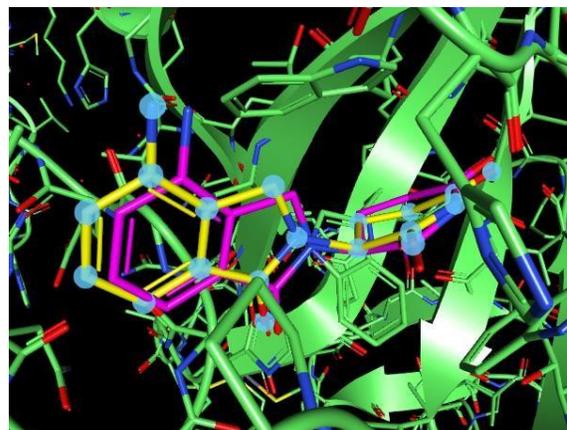
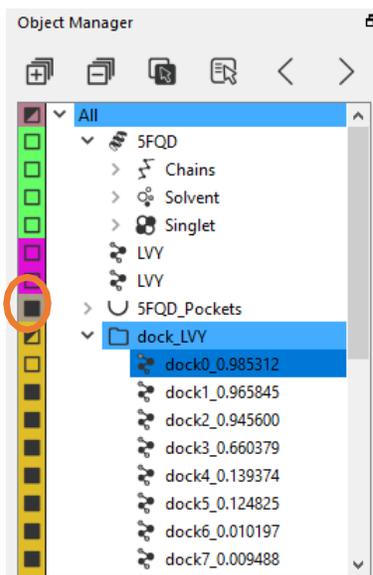
- In the **Ligand** tab select **Dock Wizard** using **dock all pocket mode**. The wizard will open a panel on the right side of the screen. Ensure that the flexible dihedral, flexible within ring structure, and Dock all boxes are checked. When ready, select Dock Begin. A new folder in the Object Manager will be created called dock\_LVY under the object SFQD\_Pockets. Right click the highlighted folder and under the Color Manager Dropdown change the color to yellow.



10. Hide the SFQD\_Pockets object in the Object Manager by selecting the square to the left of the name. Then select top docking pose named dock0 with the scroll button to center the object in the view.



11. In the Object Manager, select the black box to the left of the name of the original LVY ligand in order to display it in the screen (in purple below).



12. Select both the first docked ligand and the original ligand LVY. In the **Ligand** tab select **RMSD**. The RMSD

