Self guided Tour

Reaxys Medicinal Chemistry

WHICH SUBSTANCES ARE DUAL INHIBITORS OF TARGETS?

REAXYS® Medicinal Chemistry

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1.1 Scenario

Dual inhibitors of PI3K/mTOR?

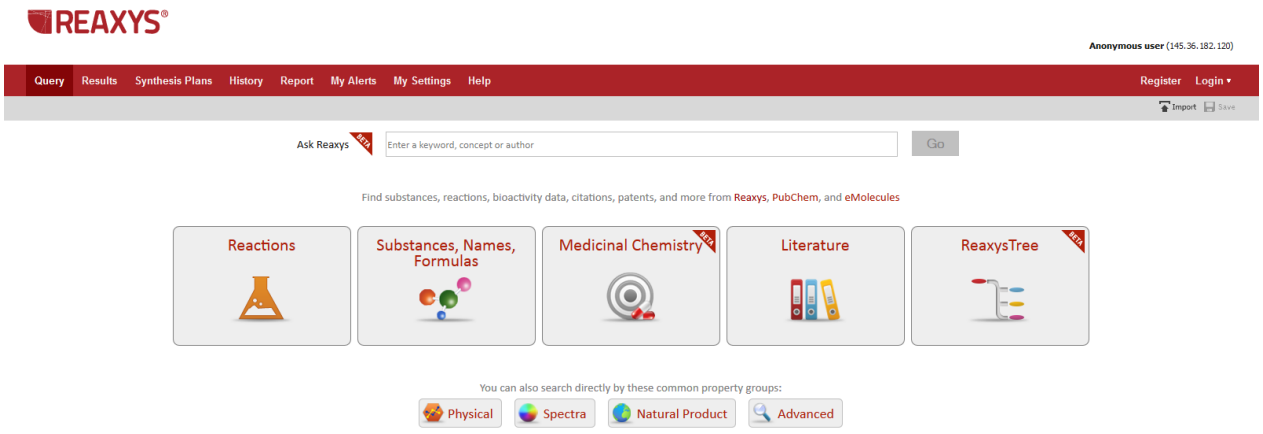
The phosphatidylinositol-3-kinase (PI3K)/AKT/mTOR signaling pathway is a central regulator in cell proliferation, growth, and angiogenesis. Inhibition of this pathway therefore is a major strategy for cancer chemotherapy. In order to induce the maximal therapeutic outcome in cancer treatment, development of dual inhibitors of PI3K and mTOR is of great interest..

Search for inhibitors active on PI3K and mTOR (FRAP)?

1.2 Overview

Major Steps	Steps and description	Action
1	Search by Bioactivity	Click 'Bioactivity' button
2	Select 'Target Name'	Type PI3K' in the 'Target Name' field and select PI3K', and Select pX>8 then push 'Search Bioactivities' button
3	Select 'Target Name'	Type 'mTOR' in the 'Target Name' field and select 'mtorc1' And 'mtorc2'and Select pX>8 then push 'Search Bioactivities' button
4	Go to the History menu	Select substance on the two queries and click on combine hitset. Select Overlap.
5	Click on the Heatmap Tab	Select the PI3K and mTORC1 and mTORC2

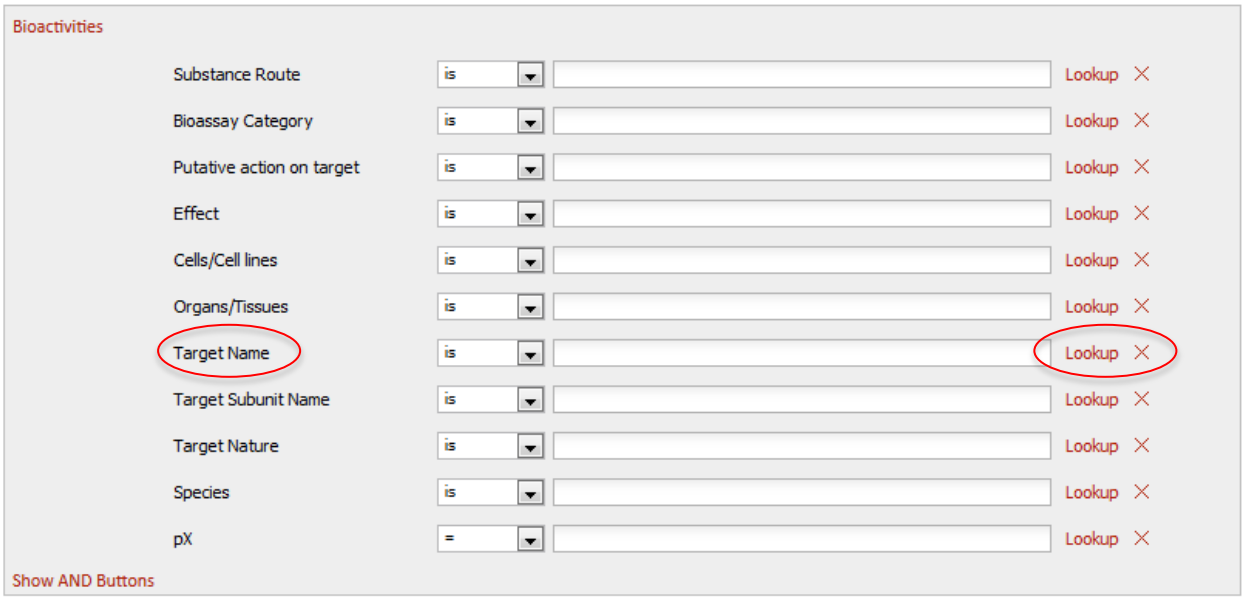
1.3 Step by step



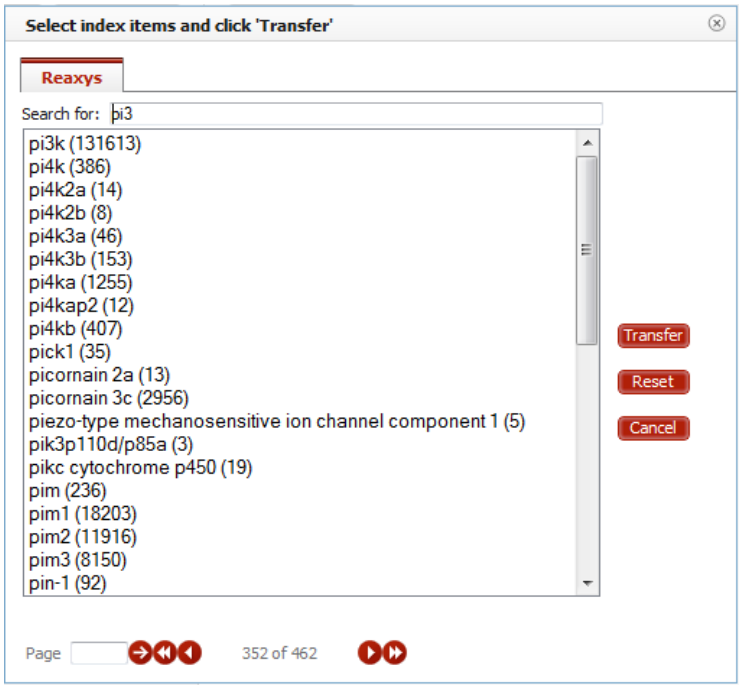
Step 1 Search Medicinal Chemistry

Step 2 Select a Target

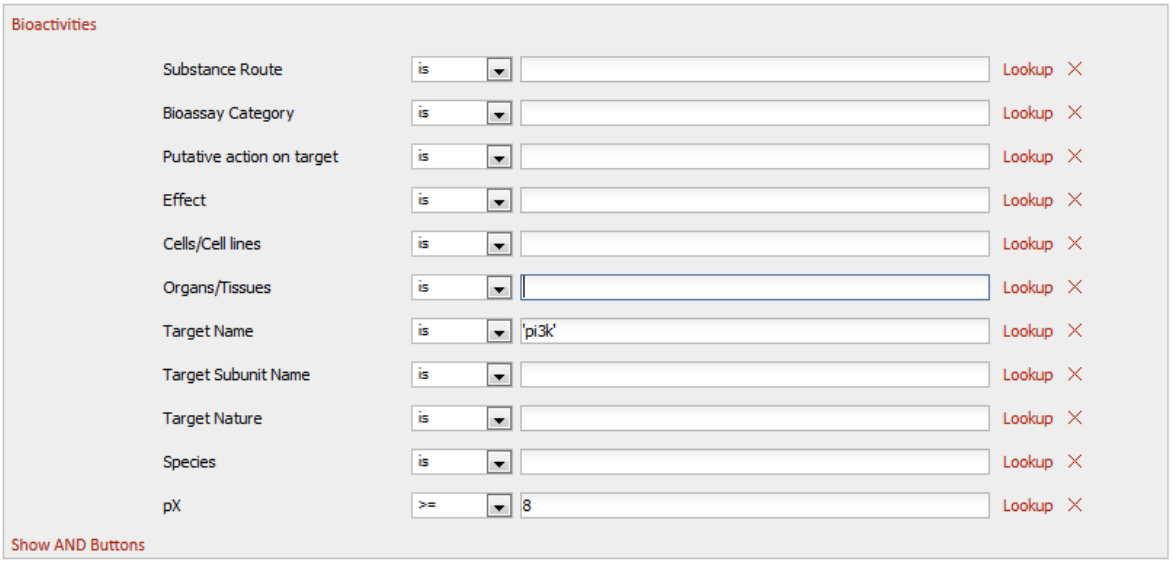
On target Name click on “look up”



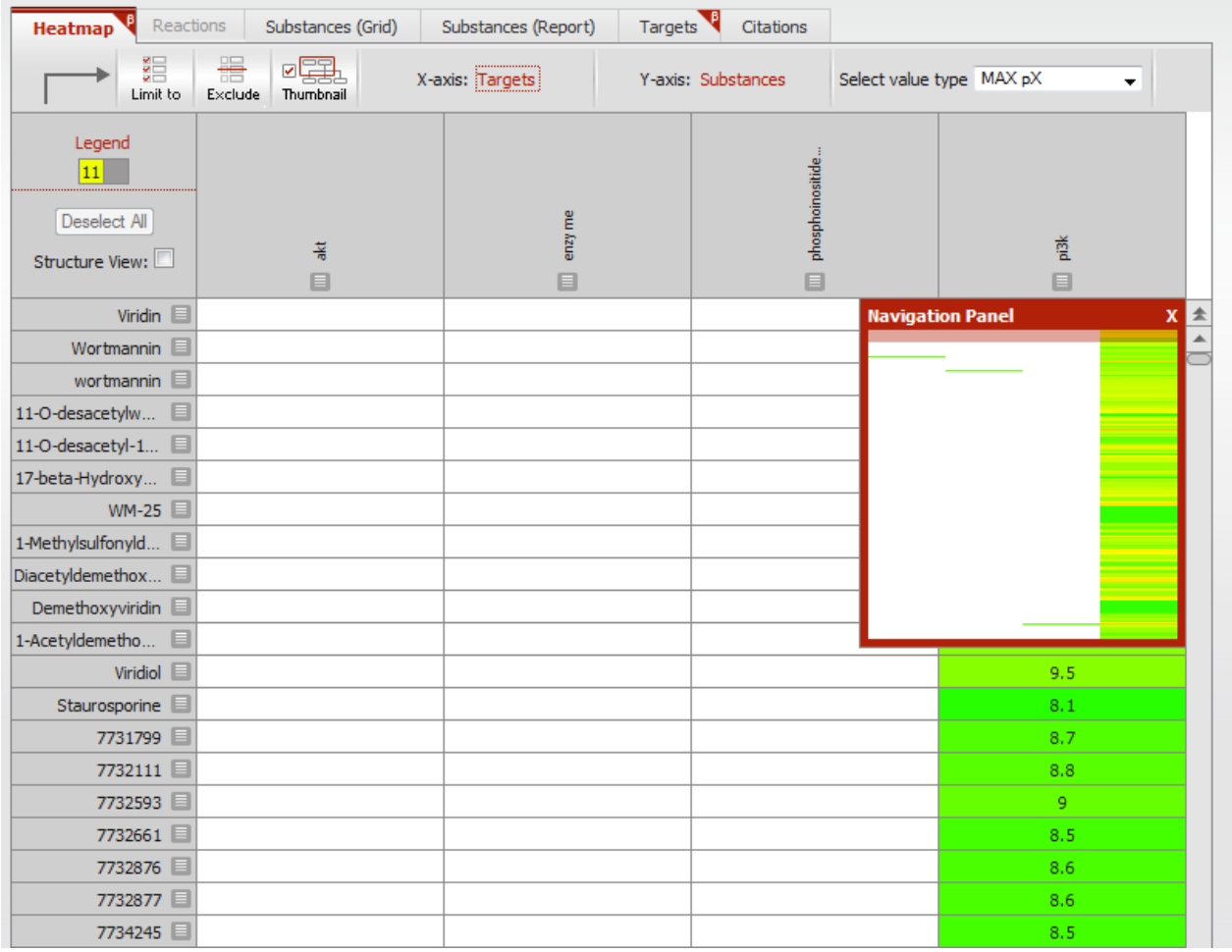
A new popup appear and Search for PI3K
Select PI3K and Click on transfer



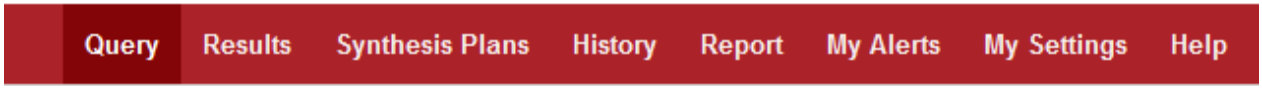
Then select >= in the pX querylet and enter 8 (Affinity less than 10 nM)



Step 3 : Search for bioactivities an Heatmap appears with PI3K potent inhibitors

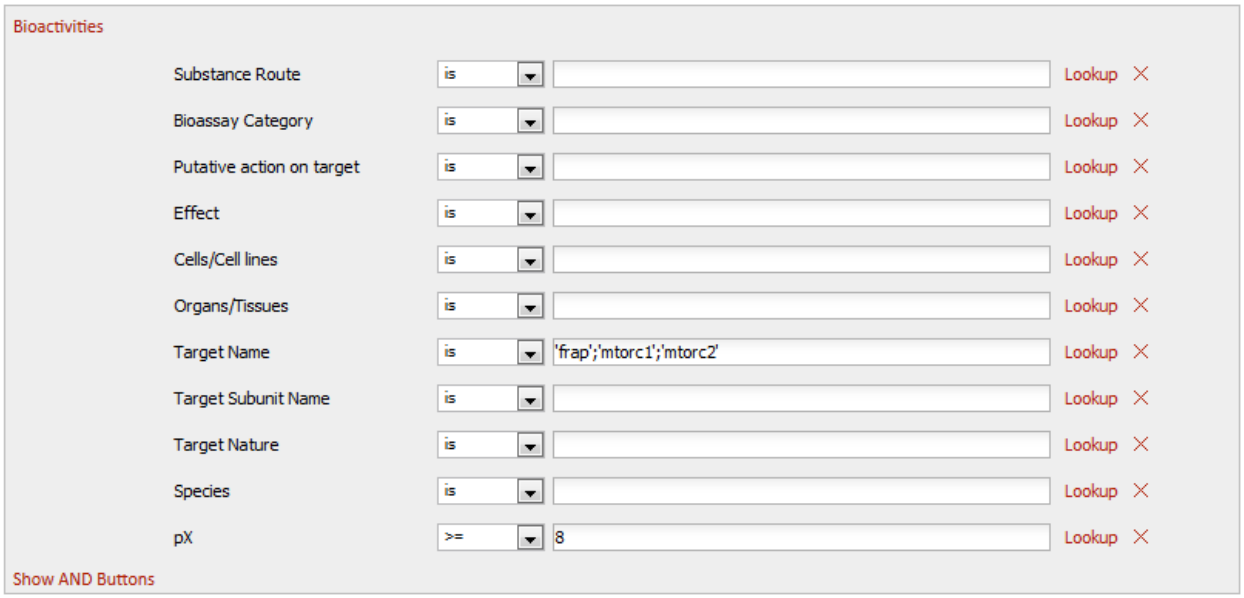


Step 4 : Go Back to the query and search for Substances tested on mTOR

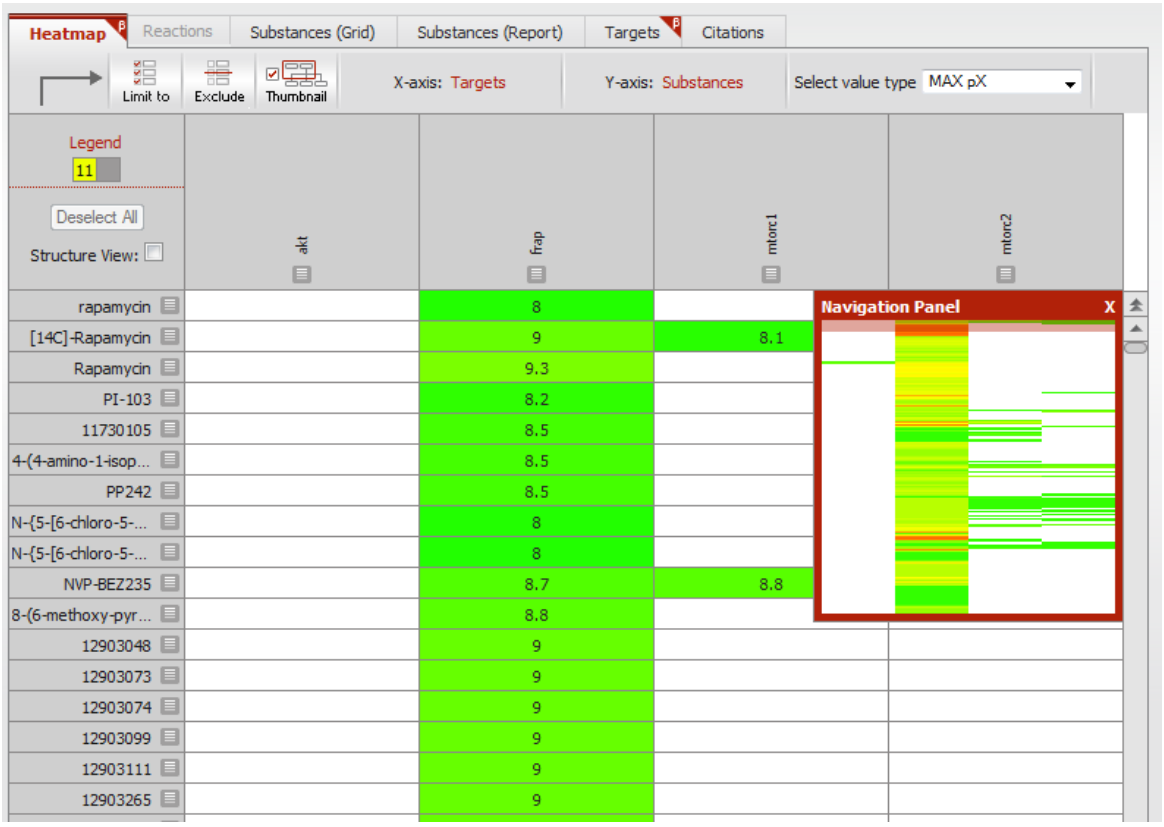


Step 5 Select a Target Name

On Target Name click on “look up” type mTOR and Select ‘mtorc1’ and mtorc2 then Click on transfer.
Click again on look up and type FRAP then select FRAP and click on transfer.
Select >= in the pX querylet and enter 8 (Affinity less than 10 nM)

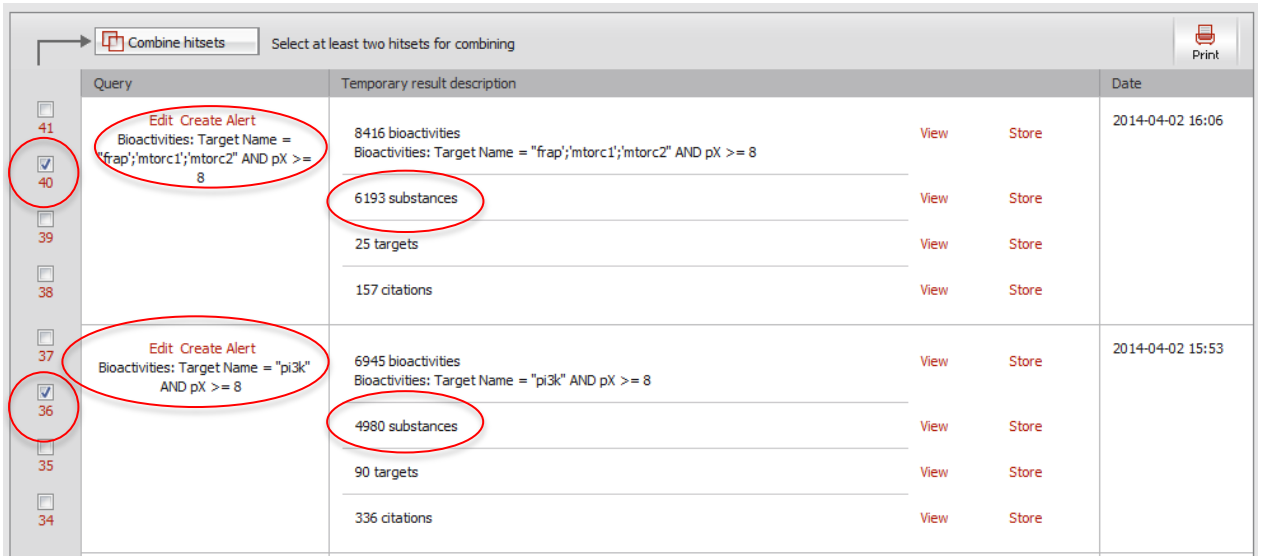


Step 6 : Search for bioactivities an Heatmap appears containing mTOR (FRAP) potent inhibitors

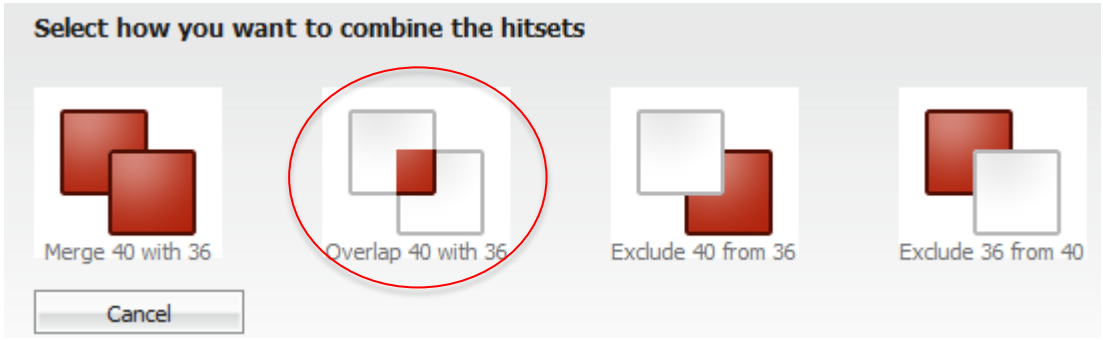


Step 7 : Go to the History and combine Hitsets

For each query select the substances and click on combine hitsets



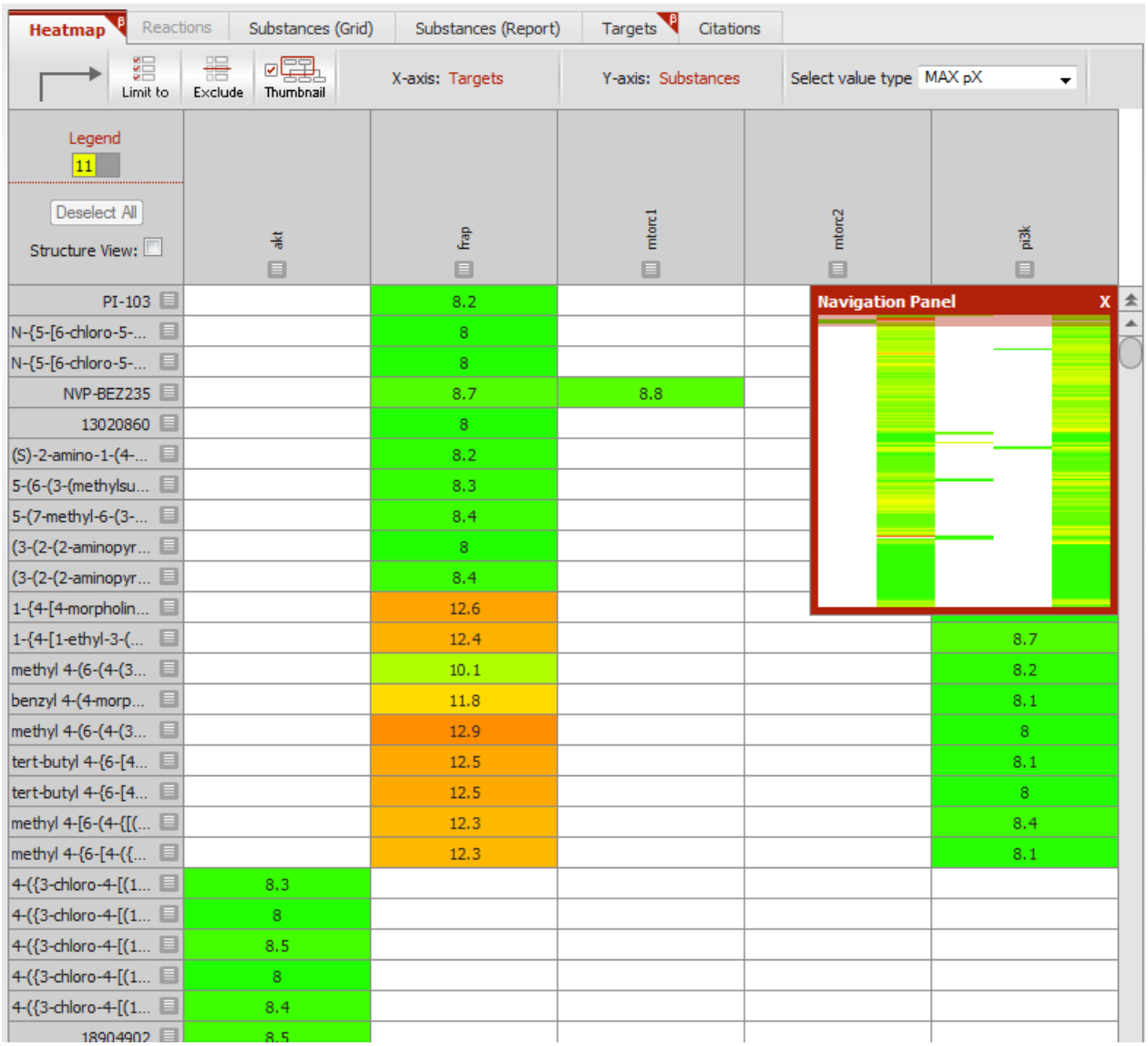
Click on overlap to retrieve dual inhibitors of PI3K and mTOR(FRAP)



Click then on the Heatmap tab

Step 9 : Dual inhibitors of mTOR(FRAP) and Pi3K

The following Heatmap displays dual inhibitors of mTOR(FRAP) and PI3K (Affinity >= 10nM)



"Two hits are better than one: targeting both phosphatidylinositol 3-kinase and mammalian target of rapamycin as a therapeutic strategy"

For more information please Contact

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