What is known about My Substance of Interest?

An Apoptosis inducer 'chemotype' from a cell- and caspase-based apoptosis high-throughput screening was found (Compound 1). A structure activity relationship expansion lead to compound 2 (Schema1).

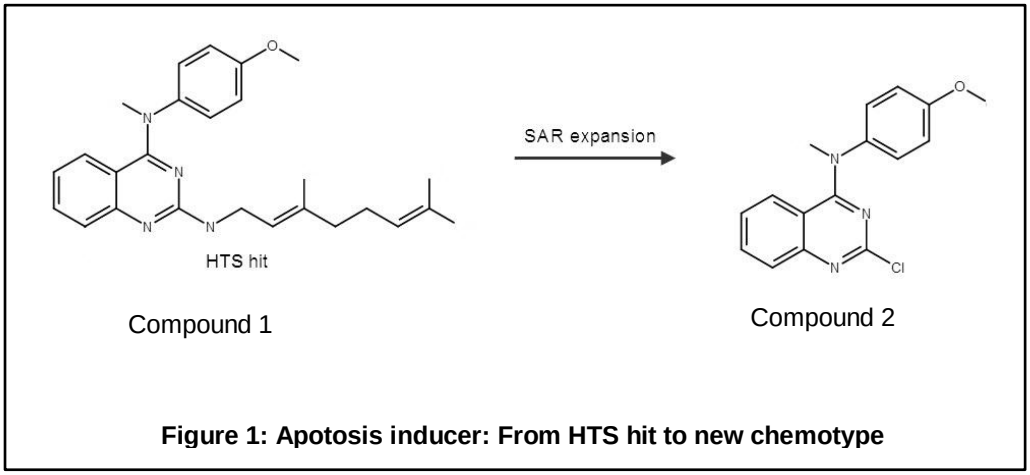


Figure 1: Apotosis inducer: From HTS hit to new chemotype

What is known about this chemotype/template (Compound 2) in Reaxys Medicinal Chemistry?

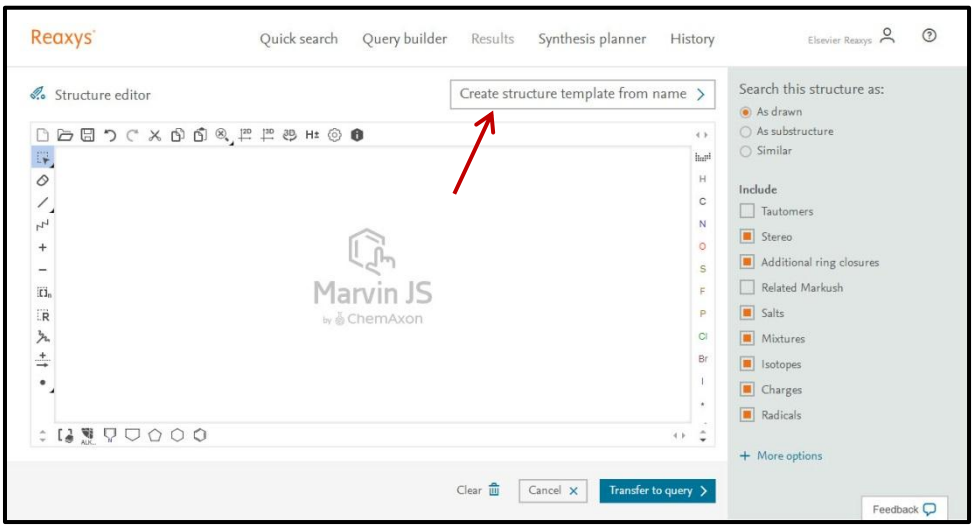
In this workflow we show examples that include:

- How to define search query, including how to search by substances and chemical drawings
- How to view substance results
- How to view Bioactivity details
- How to view a Heatmap
- How to view the profile of Compound 2 on Cell Lines
- How to view Target details

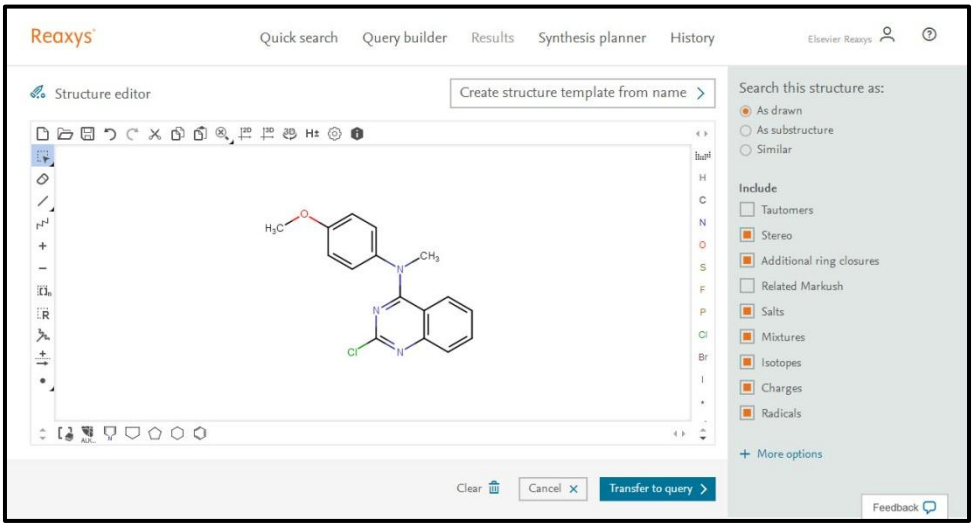
❖ Define Search Query

1. On the Reaxys home page click the ***Create Structure or Reaction Drawing*** box to open the structure editor (Marvin JS from ChemAxon).

2. Use one of the following options to draw or obtain the structure in Marvin JS:
    a. Click ***Create structure template from name***.
        i In order to save time drawing the compound, in the "*Enter a chemical name, CAS-RN, InChiKey or SMILES*" field paste the following SMILES: ***COC1=CC=C(C=C1)N(C)C1=NC(Cl)=NC2=C1C=CC=C2***
    b. Draw the compound.
        i For more information on how to use the Marvin JS structure editor, view our Structure Drawing Workflow or our How to create a Structure Drawing in Reaxys Video Tutorial.

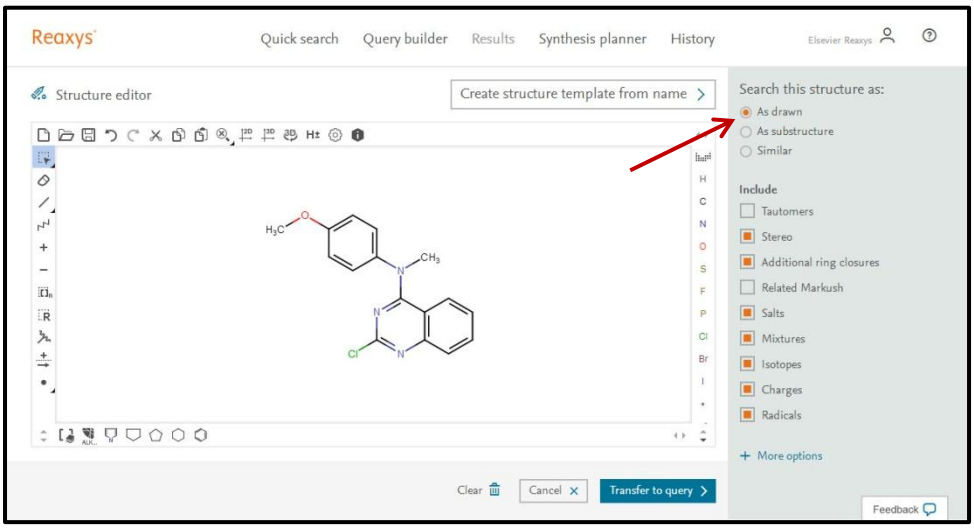


The query looks like this:

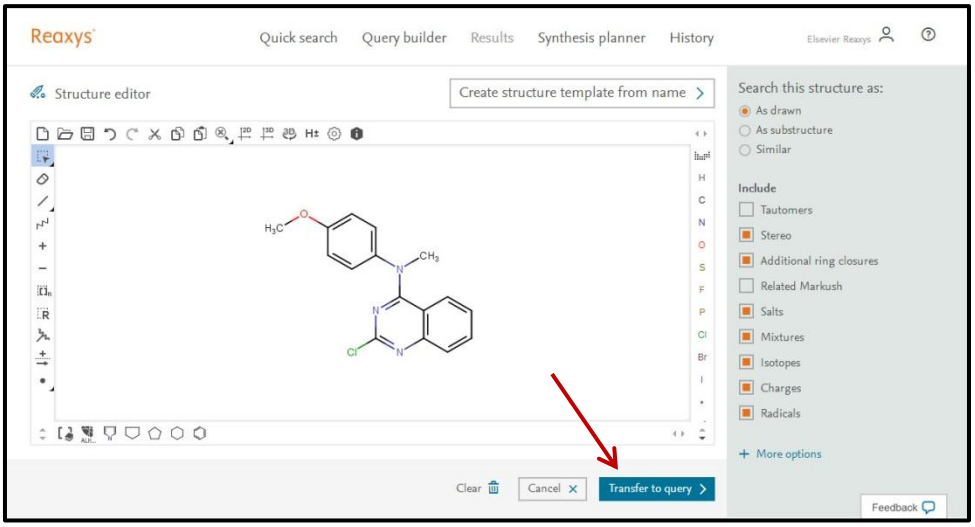


3. In the **Search this structure as**: panel, there are three options.
    - **As drawn**: Reaxys will find results for the query as drawn
    - **As substructure**: Reaxys offers two sub-options:
        - **On all atoms** will substitute any explicit or implicit hydrogen with any other atom or group
        - **On heteroatoms** will do the same but only on heteroatoms
    - **Similar***:* Reaxys will find results for a similarity search based on the drawn query

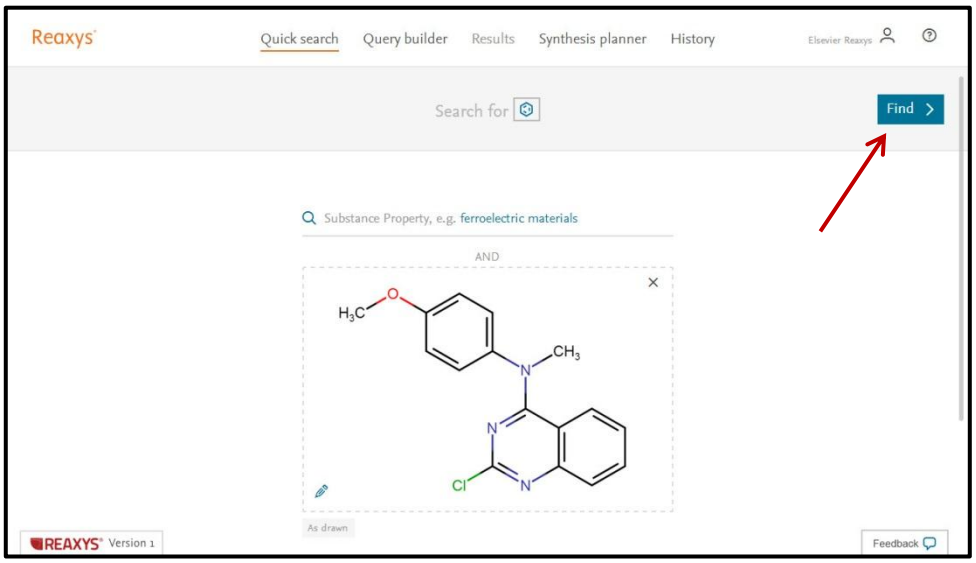
    a. If necessary, click ***As drawn*** to run an exact search on Compound 2.



4. Click ***Transfer to query***

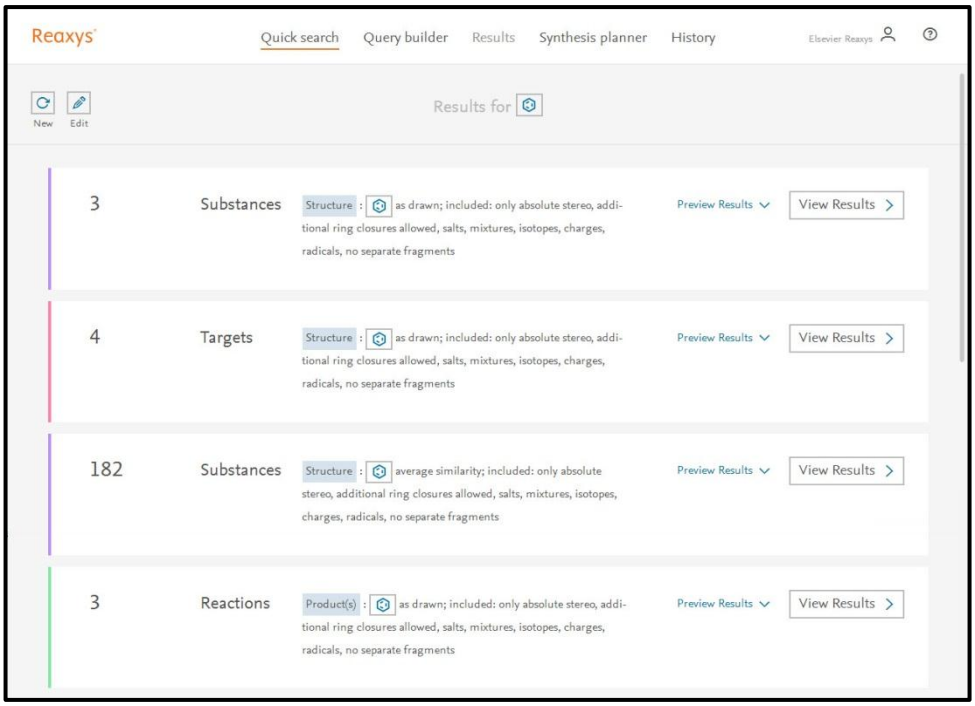


5. Click ***Find***.



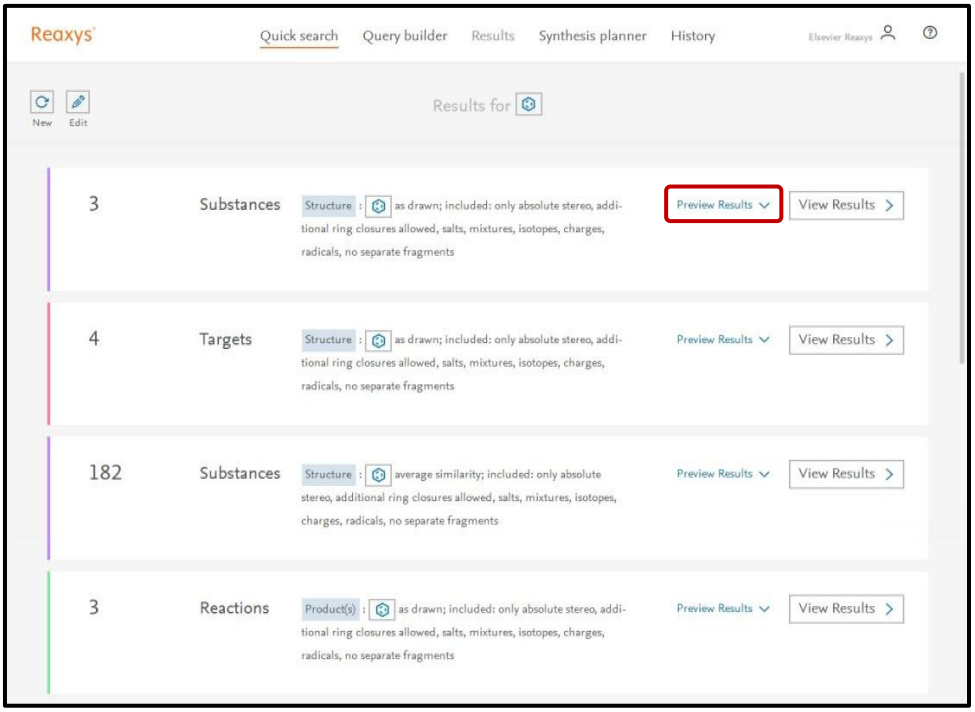
The Results Preview is displayed.

- Reaxys will present a Results Preview showing different variations of the entered query to provide you with options, which you may not have thought of at query formulation time:
  - Substance Results for the drawn query
  - Target Results for the drawn query
  - Substance Results for a similarity search based on the drawn query
  - Reaction Results for the drawn query

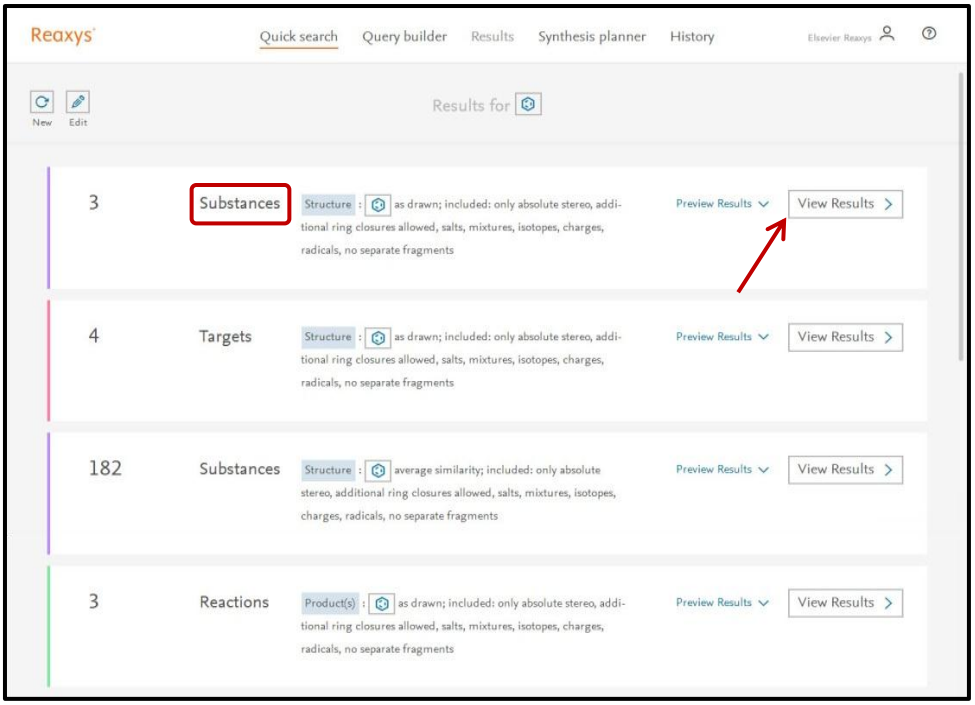


❖ View Results

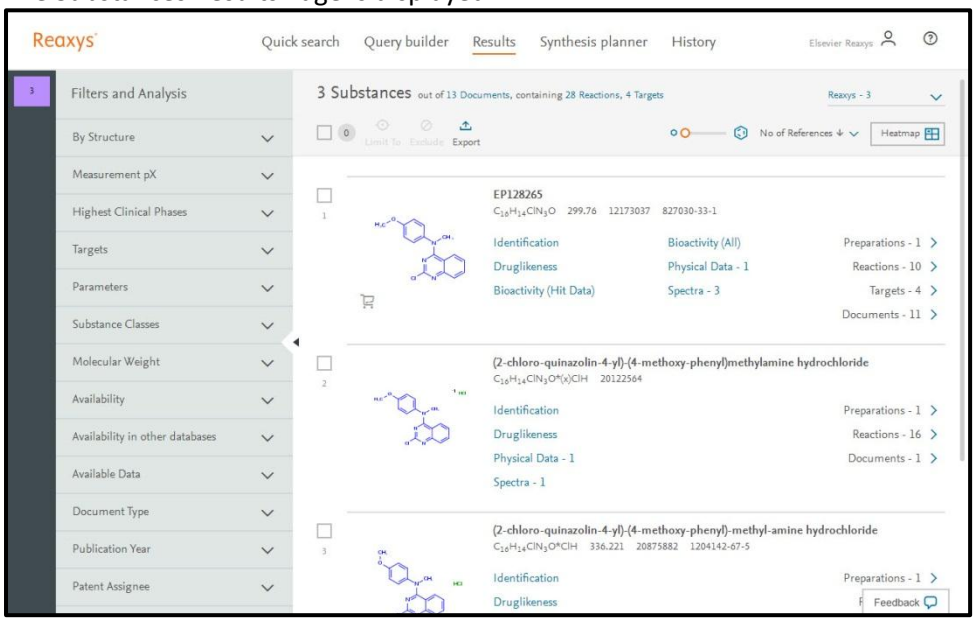
Each result set has a **Preview Results** feature that presents the top three results for the given query. You can check these top results before continuing to the full result set.



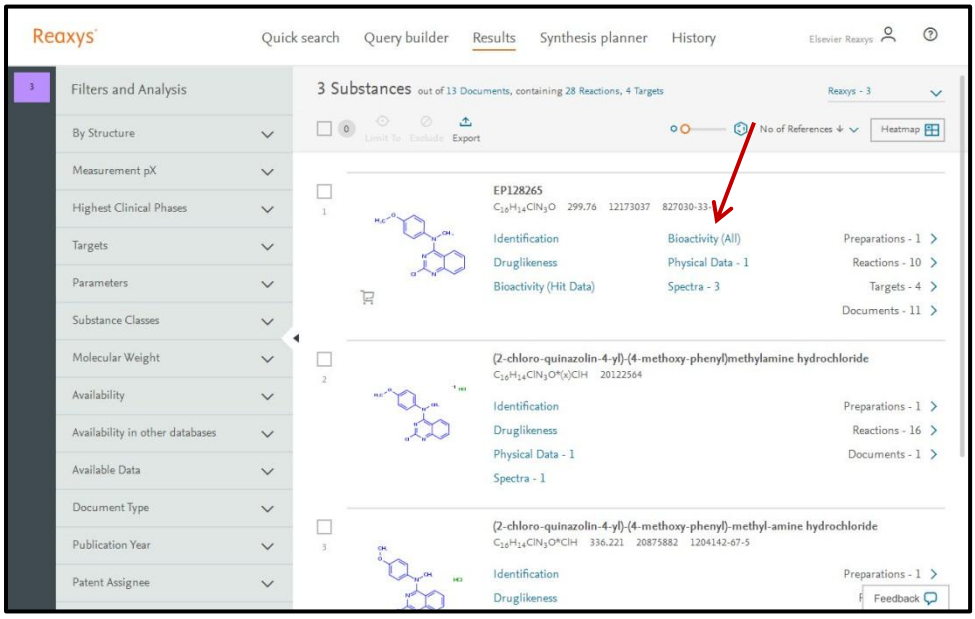
1. Click ***View Results*** for the first result set (Substances – as drawn).



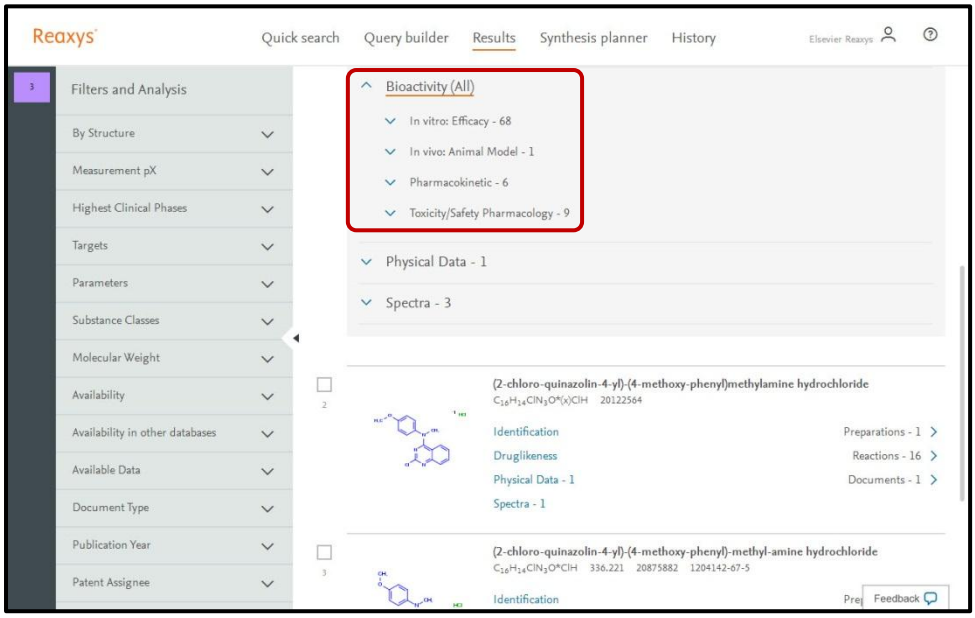
The Substances Results Page is displayed.



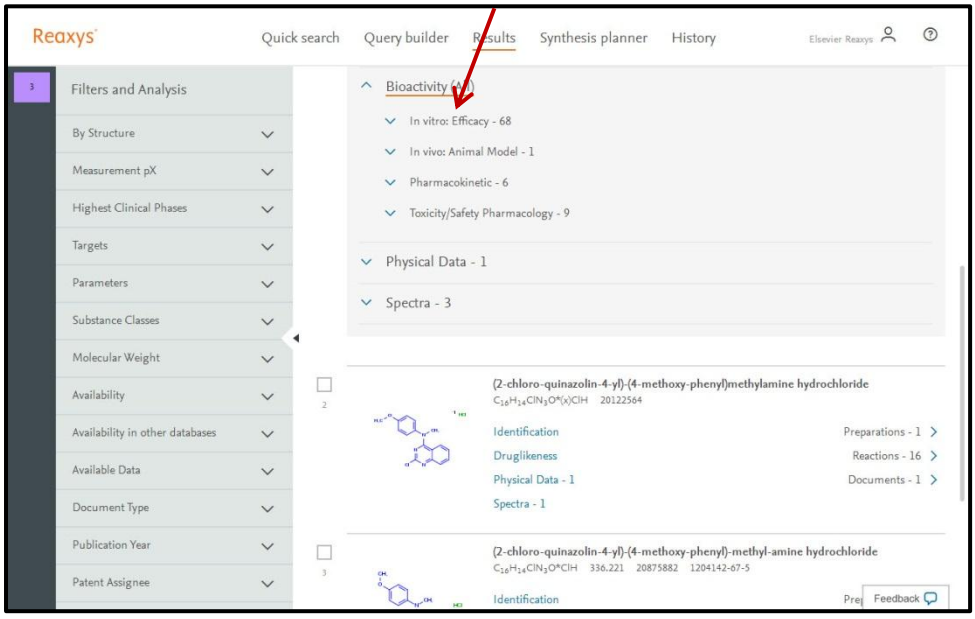
2. Click ***Bioactivity (All)*** for the first substance to view the Bioactivities



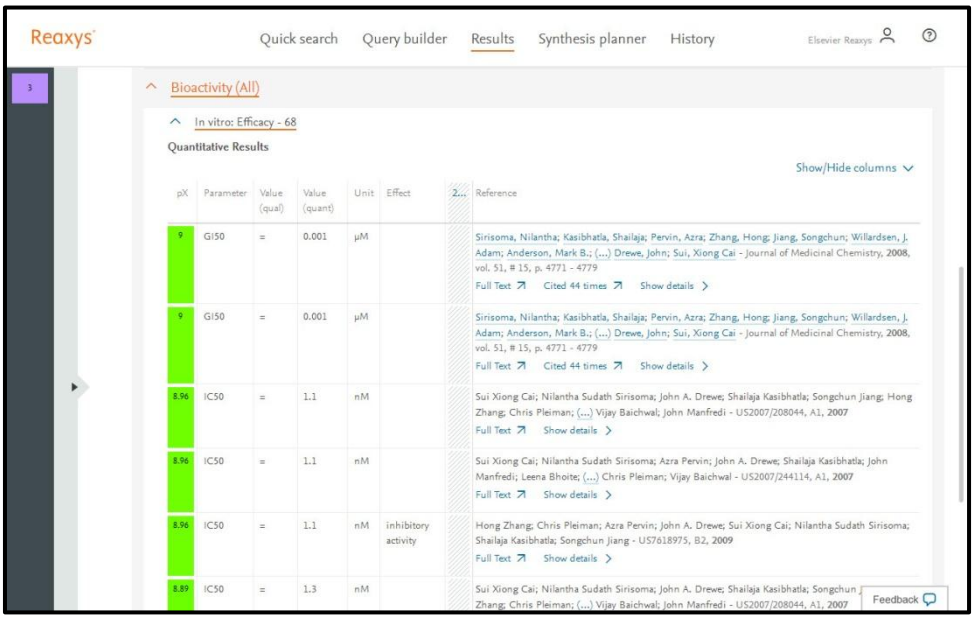
The Bioactivity Categories are displayed:



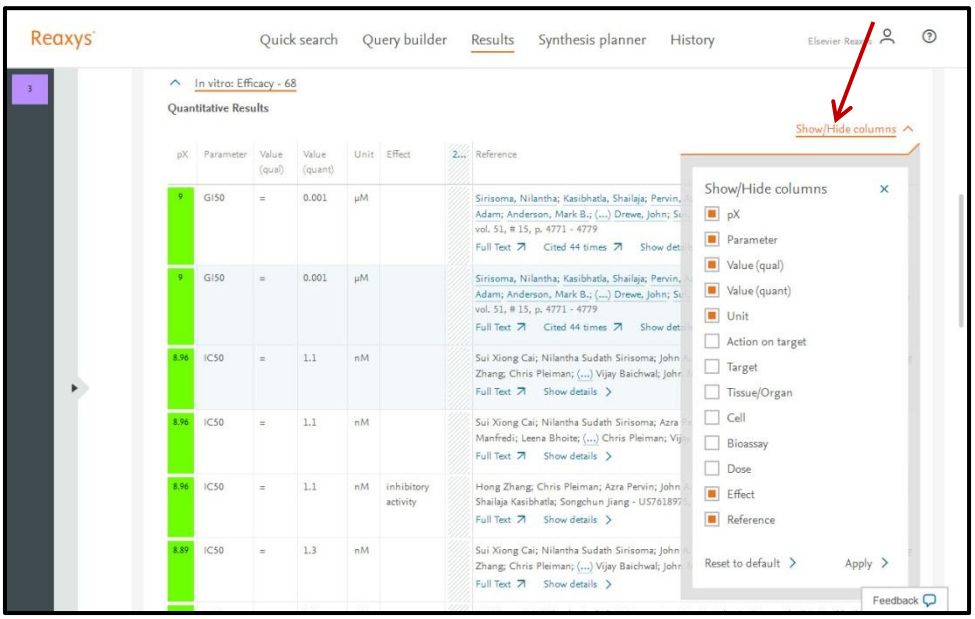
3. Click a category, such as ***In vitro: Efficacy*** to display the corresponding bioactivities.



The results are displayed in table view when the results are quantitative (shown below) and in a text view when qualitative.

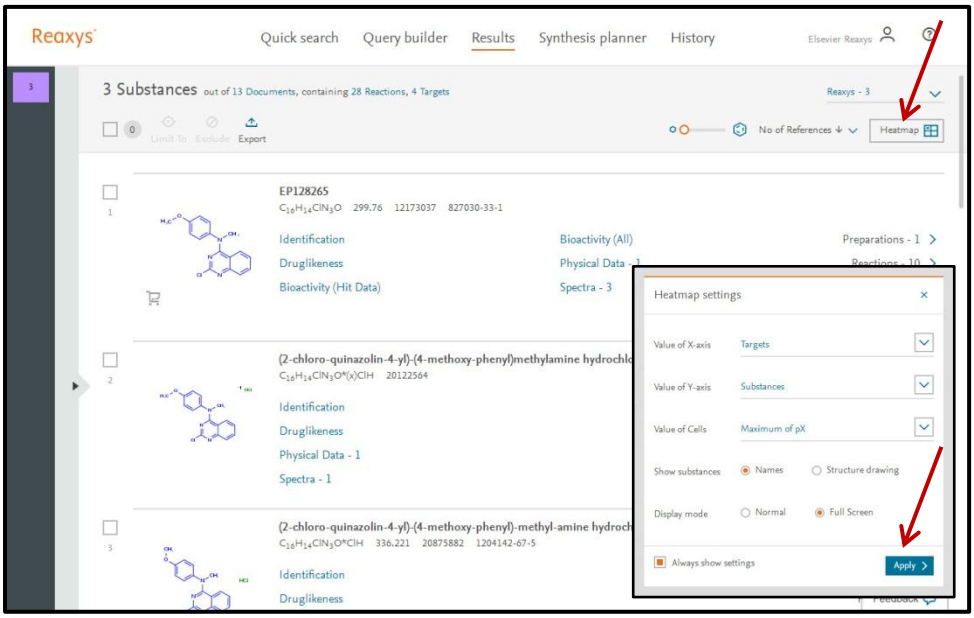


4. Click ***Show/Hide columns*** to manage column display.



❖ View the Heatmap

1. Scroll to the top and click ***Heatmap***.
   a. Review the Settings and click ***Apply***.

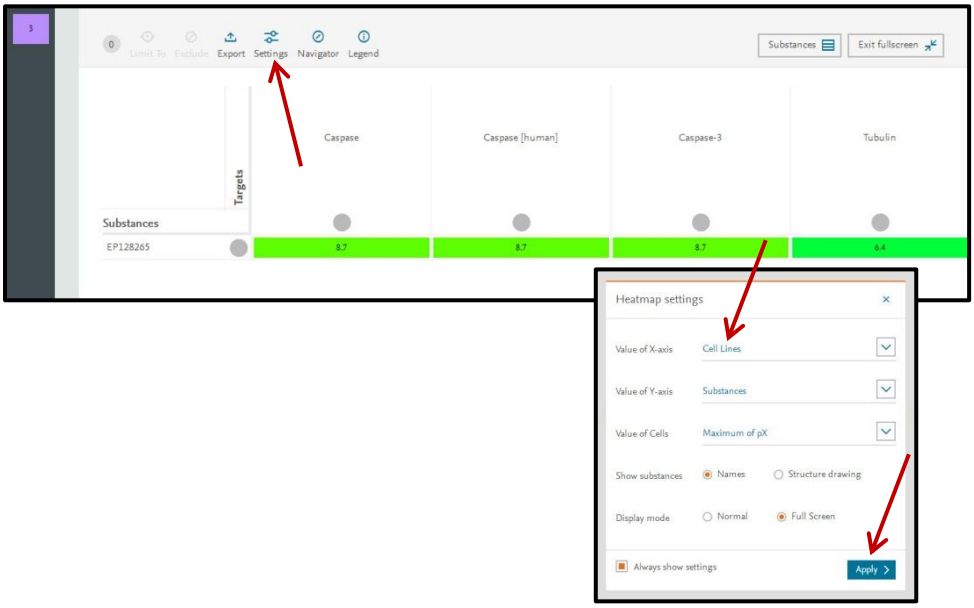


The Heatmap is displayed which provide a profile of target hits by the corresponding compound.

   b. Click ***Legend*** to display the legend. Color indicates bioactivity potency based on pX value. The number indicates the pX value.

Compound 2 is an anti-proliferative agent that was probably tested as an inhibitor of cell proliferation on well-known cell lines. Let's look at how a cell line profile can be retrieved with Reaxys Medicinal Chemistry for compound 2?

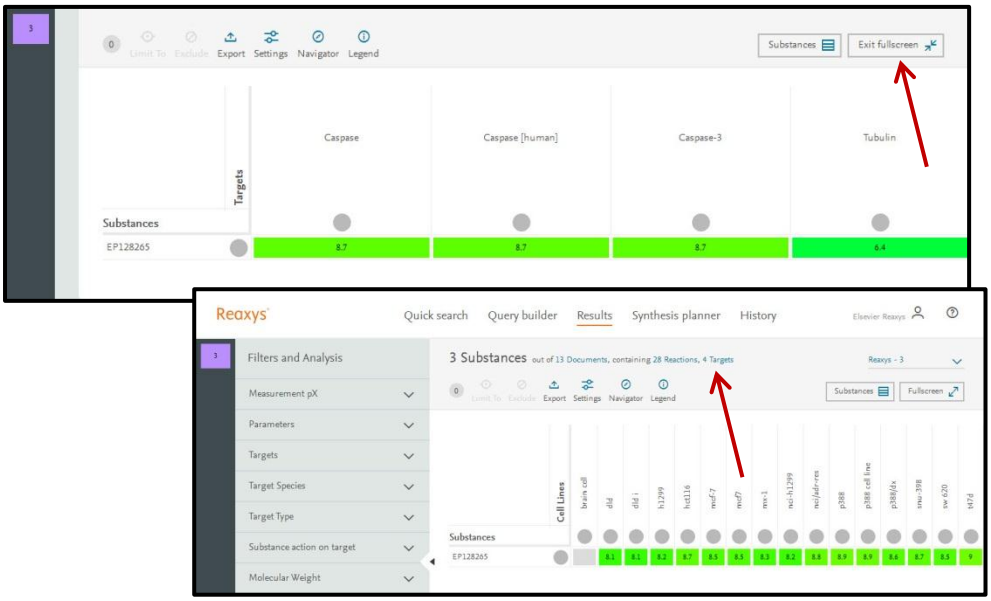
2. Click **Settings**.
    a. Change ***Value of X-axis*** *to* ***Cell Lines***
    b. Click ***Apply***.



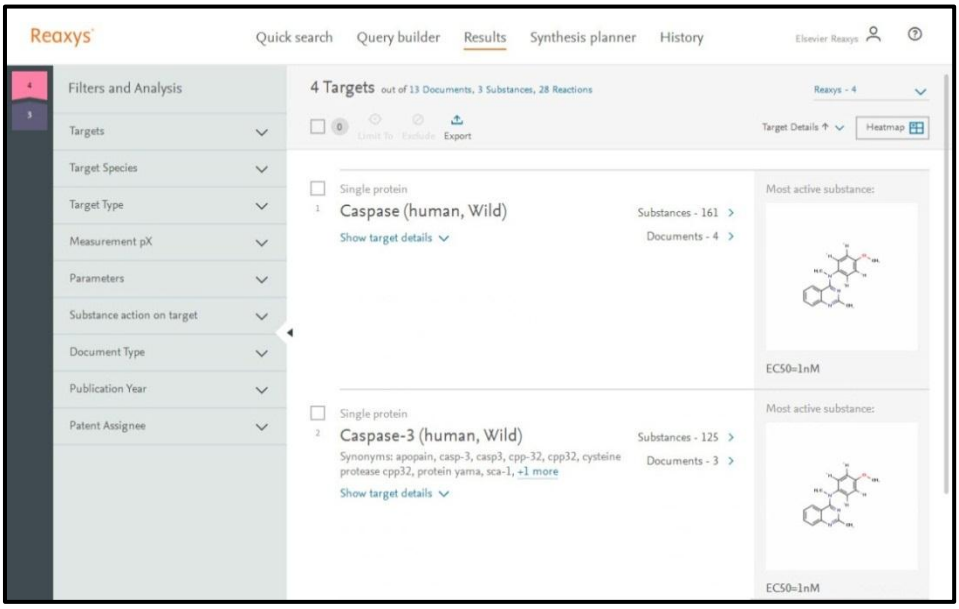
A profile on Cell lines appears in the Heatmap view.

❖ View Target Details

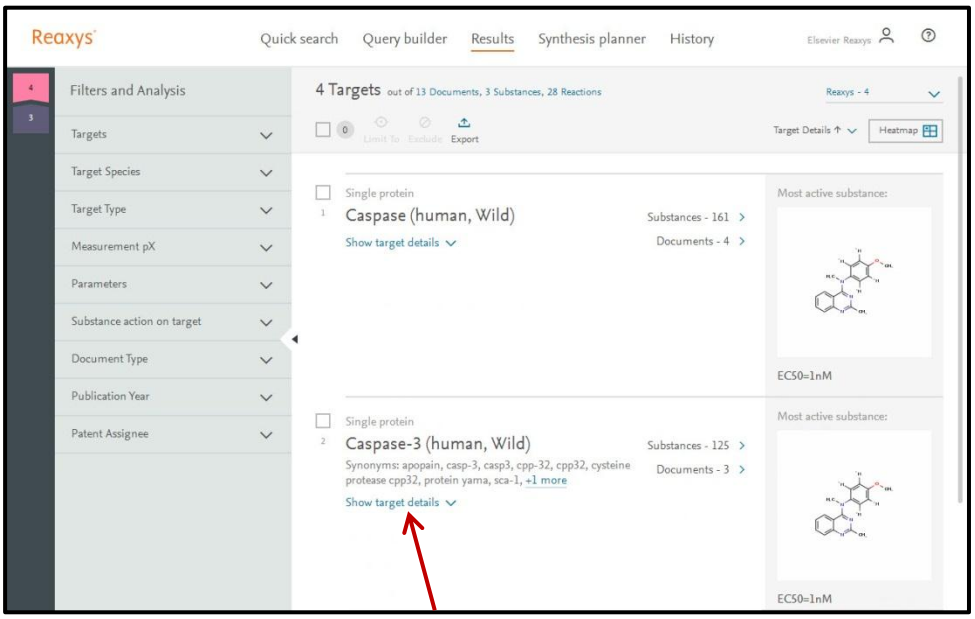
1. Click ***Exit fullscreen***.
    a. Click ***4 Targets***.



The Targets Results Page is displayed with details on each target.



2. Click ***Show target details*** for the 2nd results.



The Target details are displayed and include information on which *Bioassays* and/or *Cell lines* were used to generate the corresponding bioactivities on the Caspase-3 (human, Wild).