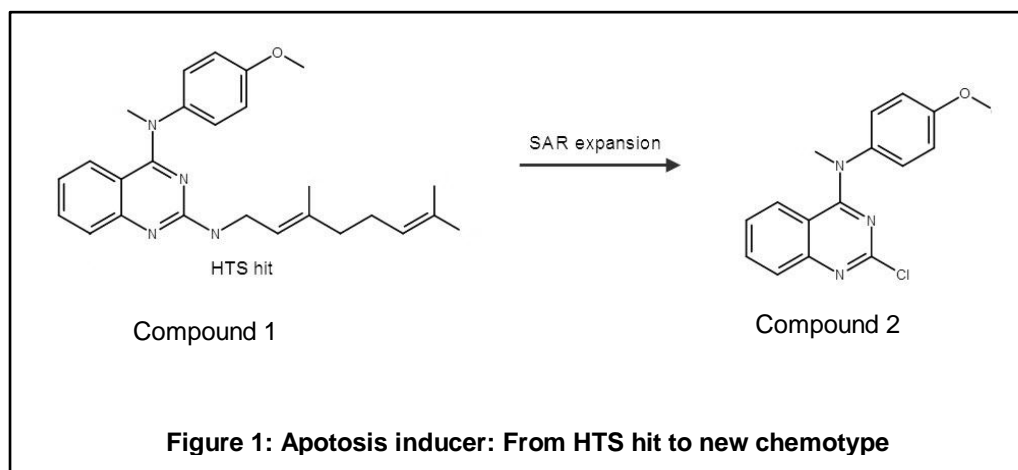


## What is known about My Substance of Interest?

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).



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

In this workflow we show examples that include:

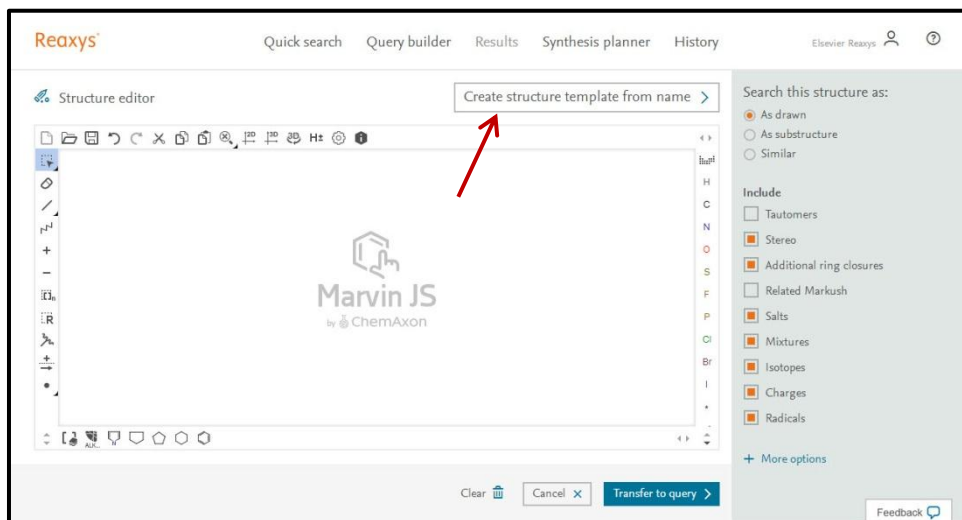
- How to define search query, including how to search by substances and chemical drawings
- How to view substance results
- How to view Bioactivity details
- How to view a Heatmap
- How to view the profile of Compound 2 on Cell Lines
- How to view Target details

### ❖ Define Search Query

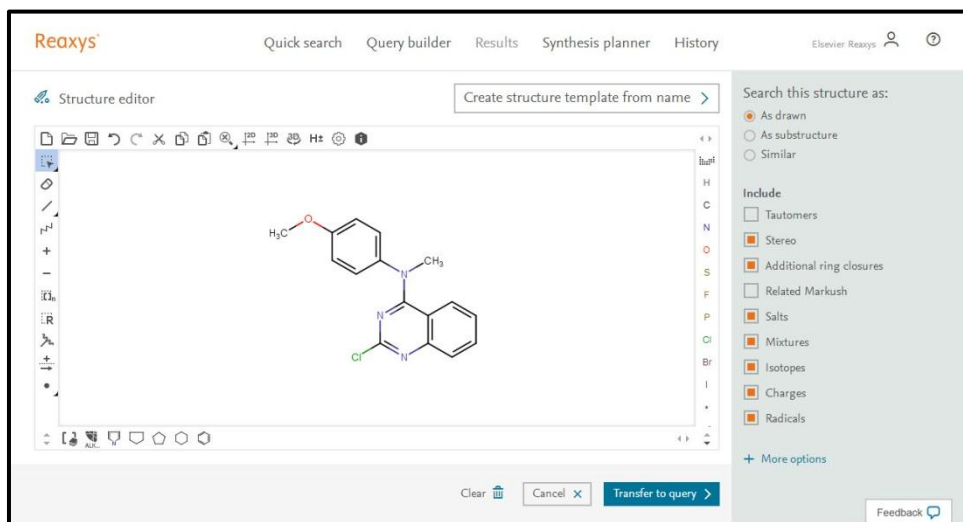
1. On the Reaxys home page click the **Create Structure or Reaction Drawing** box to open the structure editor (Marvin JS from ChemAxon).



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(CI)=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:



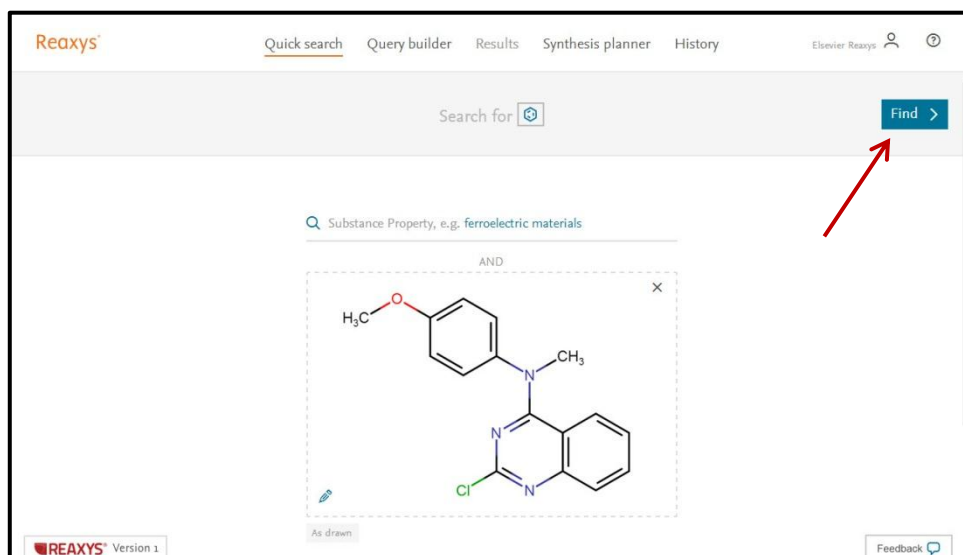
3. In the **Search this structure as:** panel, there are three options.
  - **As drawn:** Reaxys will find results for the query as drawn
  - **As substructure:** Reaxys offers two sub-options:
    - **On all atoms** will substitute any explicit or implicit hydrogen with any other atom or group
    - **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.

The screenshot shows the Reaxys 'Structure editor' interface. The main window displays a chemical structure of a quinoline derivative with a methoxy group and a methyl group. On the right side, the 'Search this structure as:' panel is open, showing three radio button options: 'As drawn' (selected), 'As substructure', and 'Similar'. Below these are various 'Include' options like 'Tautomers', 'Stereo', 'Additional ring closures', etc. A red arrow points to the 'As drawn' radio button.

4. Click **Transfer to query**

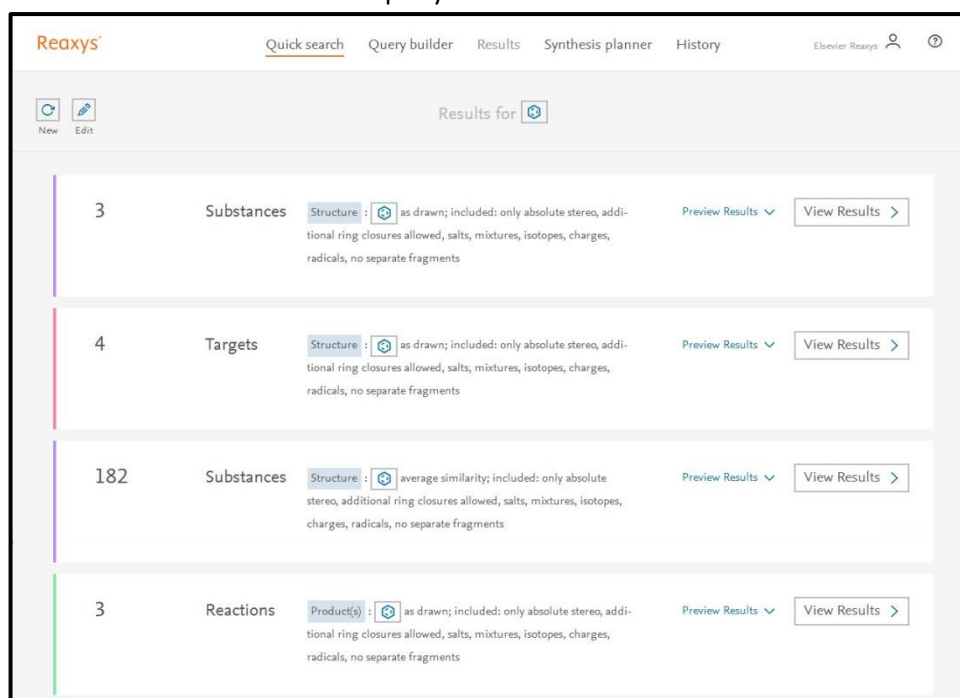
This screenshot is identical to the previous one, showing the same chemical structure and search options. A red arrow now points to the 'Transfer to query' button located at the bottom of the interface, below the 'Cancel' button.

## 5. Click **Find**.



The Results Preview is displayed.

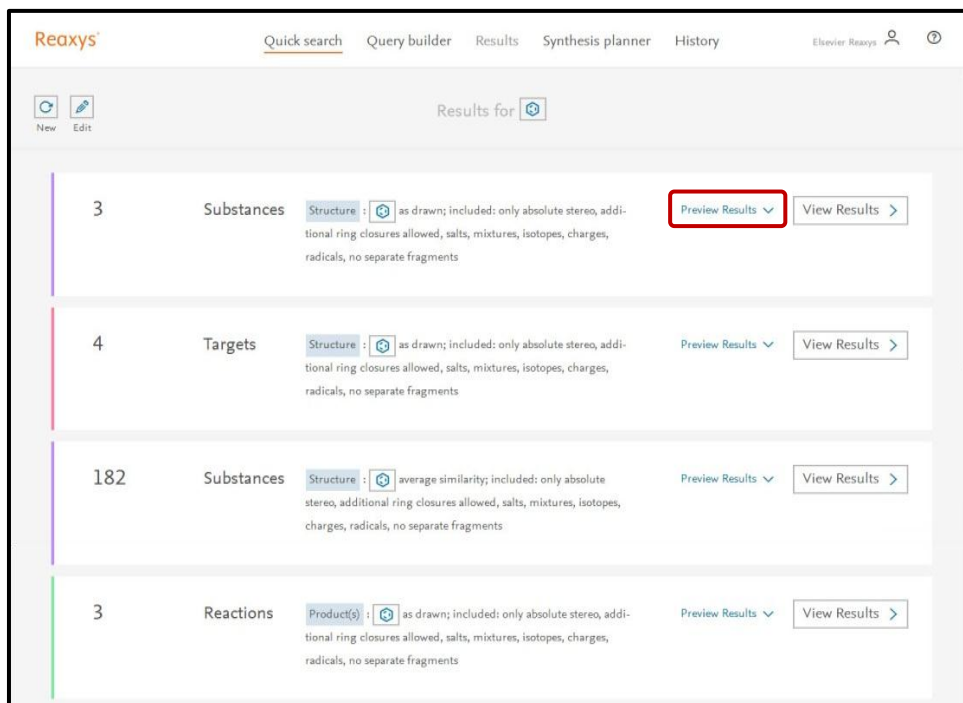
- Reaxys will present a Results Preview showing different variations of the entered query to provide you with options, which you may not have thought of at query formulation time:
  - Substance Results for the drawn query
  - Target Results for the drawn query
  - Substance Results for a similarity search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



Count	Category	Structure	Search Filter	View Results
3	Substances	Structure	as drawn; included: only absolute stereo, additional ring closures allowed, salts, mixtures, isotopes, charges, radicals, no separate fragments	View Results >
4	Targets	Structure	as drawn; included: only absolute stereo, additional ring closures allowed, salts, mixtures, isotopes, charges, radicals, no separate fragments	View Results >
182	Substances	Structure	average similarity; included: only absolute stereo, additional ring closures allowed, salts, mixtures, isotopes, charges, radicals, no separate fragments	View Results >
3	Reactions	Product(s)	as drawn; included: only absolute stereo, additional ring closures allowed, salts, mixtures, isotopes, charges, radicals, no separate fragments	View Results >

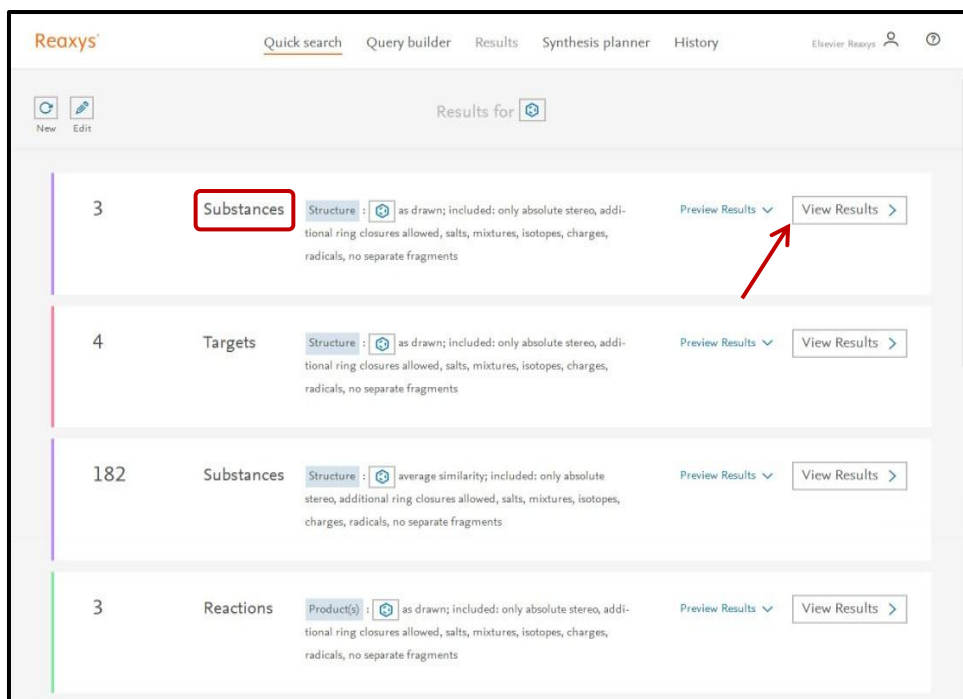
## ❖ View Results

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.



The screenshot shows the Reaxys search results interface. At the top, there are navigation tabs: Quick search, Query builder, Results, Synthesis planner, and History. Below the navigation, there are icons for 'New' and 'Edit'. The main content area displays four result sets, each with a count, a category, a structure type, and a 'Preview Results' button. The first result set is 'Substances' with a count of 3, and its 'Preview Results' button is highlighted with a red box. The other result sets are 'Targets' (4), 'Substances' (182), and 'Reactions' (3).

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



This screenshot is identical to the previous one, but with a red box around the 'Substances' category of the first result set and a red arrow pointing to the 'View Results' button, indicating the next step in the process.

The Substances Results Page is displayed.

Reaxys® Quick search Query builder **Results** Synthesis planner History Elsevier Reaxys

3 Filters and Analysis

3 Substances out of 13 Documents, containing 28 Reactions, 4 Targets

By Structure Measurement pK Highest Clinical Phases Targets Parameters Substance Classes Molecular Weight Availability Availability in other databases Available Data Document Type Publication Year Patent Assignee

1 **EPI28265**  
C18H14ClN3O 299.76 12173037 827030-33-1  
 Identification Bioactivity (All) Preparations - 1 >  
 Druglikeness Physical Data - 1 Reactions - 10 >  
 Bioactivity (Hit Data) Spectra - 3 Targets - 4 >  
 Documents - 11 >

2 **[2-chloro-quinazolin-4-yl)-(4-methoxy-phenyl)methylamine hydrochloride**  
C18H14ClN3O\*(Cl)Cl 20122564  
 Identification Preparations - 1 >  
 Druglikeness Reactions - 16 >  
 Physical Data - 1 Documents - 1 >  
 Spectra - 1

3 **[2-chloro-quinazolin-4-yl)-(4-methoxy-phenyl)-methyl-amine hydrochloride**  
C18H14ClN3O\*(Cl)Cl 336.221 20875882 1204142-67-5  
 Identification Preparations - 1 >  
 Druglikeness Feedback

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

Reaxys® Quick search Query builder **Results** Synthesis planner History Elsevier Reaxys

3 Filters and Analysis

3 Substances out of 13 Documents, containing 28 Reactions, 4 Targets

By Structure Measurement pK Highest Clinical Phases Targets Parameters Substance Classes Molecular Weight Availability Availability in other databases Available Data Document Type Publication Year Patent Assignee

1 **EPI28265**  
C18H14ClN3O 299.76 12173037 827030-33-1  
 Identification Bioactivity (All) Preparations - 1 >  
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 Bioactivity (Hit Data) Spectra - 3 Targets - 4 >  
 Documents - 11 >

2 **[2-chloro-quinazolin-4-yl)-(4-methoxy-phenyl)methylamine hydrochloride**  
C18H14ClN3O\*(Cl)Cl 20122564  
 Identification Preparations - 1 >  
 Druglikeness Reactions - 16 >  
 Physical Data - 1 Documents - 1 >  
 Spectra - 1

3 **[2-chloro-quinazolin-4-yl)-(4-methoxy-phenyl)-methyl-amine hydrochloride**  
C18H14ClN3O\*(Cl)Cl 336.221 20875882 1204142-67-5  
 Identification Preparations - 1 >  
 Druglikeness Feedback

The Bioactivity Categories are displayed:

The screenshot shows the Reaxys interface with the 'Bioactivity (All)' menu expanded. The categories listed are:

- In vitro: Efficacy - 68
- In vivo: Animal Model - 1
- Pharmacokinetic - 6
- Toxicity/Safety Pharmacology - 9
- Physical Data - 1
- Spectra - 3

The 'In vitro: Efficacy' category is highlighted with a red box. Below the menu, two chemical entries are visible, both for [2-chloro-quinazolin-4-yl]-(4-methoxy-phenyl)methylamine hydrochloride. The first entry has a count of 2 and the second has a count of 3. Each entry includes a chemical structure, identification details, and links to related information like Preparations, Reactions, Physical Data, Spectra, and Documents.

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

This screenshot is identical to the previous one, but with a red arrow pointing to the 'In vitro: Efficacy' category in the expanded menu, indicating it has been selected.

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

**Quantitative Results**

pX	Parameter	Value (qual)	Value (quant)	Unit	Effect	Reference
9	GI50	=	0.001	µM		Sirisoma, Nilantha; Kasibhatla, Shailaja; Pervin, Azra; Zhang, Hong; Jiang, Songchun; Willardsen, J. Adam; Anderson, Mark B.; (...) Drew, John; Sui, Xiong Cai - Journal of Medicinal Chemistry, 2008, vol. 51, # 15, p. 4771 - 4779 Full Text <a href="#">↗</a> Cited 44 times <a href="#">↗</a> Show details <a href="#">&gt;</a>
9	GI50	=	0.001	µM		Sirisoma, Nilantha; Kasibhatla, Shailaja; Pervin, Azra; Zhang, Hong; Jiang, Songchun; Willardsen, J. Adam; Anderson, Mark B.; (...) Drew, John; Sui, Xiong Cai - Journal of Medicinal Chemistry, 2008, vol. 51, # 15, p. 4771 - 4779 Full Text <a href="#">↗</a> Cited 44 times <a href="#">↗</a> Show details <a href="#">&gt;</a>
8.96	IC50	=	1.1	nM		Sui Xiong Cai; Nilantha Sudath Sirisoma; John A. Drew; Shailaja Kasibhatla; Songchun Jiang; Hong Zhang; Chris Pleiman; (...) Vijay Baichwal; John Manfredi - US2007/208044, A1, 2007 Full Text <a href="#">↗</a> Show details <a href="#">&gt;</a>
8.96	IC50	=	1.1	nM		Sui Xiong Cai; Nilantha Sudath Sirisoma; Azra Pervin; John A. Drew; Shailaja Kasibhatla; John Manfredi; Leena Bhoite; (...) Chris Pleiman; Vijay Baichwal - US2007/244114, A1, 2007 Full Text <a href="#">↗</a> Show details <a href="#">&gt;</a>
8.96	IC50	=	1.1	nM	inhibitory activity	Hong Zhang; Chris Pleiman; Azra Pervin; John A. Drew; Sui Xiong Cai; Nilantha Sudath Sirisoma; Shailaja Kasibhatla; Songchun Jiang - US7618975, B2, 2009 Full Text <a href="#">↗</a> Show details <a href="#">&gt;</a>
8.89	IC50	=	1.3	nM		Sui Xiong Cai; Nilantha Sudath Sirisoma; John A. Drew; Shailaja Kasibhatla; Songchun Jiang; Zhang; Chris Pleiman; (...) Vijay Baichwal; John Manfredi - US2007/208044, A1, 2007 Full Text <a href="#">↗</a> Show details <a href="#">&gt;</a>

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

**Show/Hide columns**

- pX
- Parameter
- Value (qual)
- Value (quant)
- Unit
- Action on target
- Target
- Tissue/Organ
- Cell
- Bioassay
- Dose
- Effect
- Reference

Reset to default [>](#) Apply [>](#)



## ❖ View the Heatmap

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

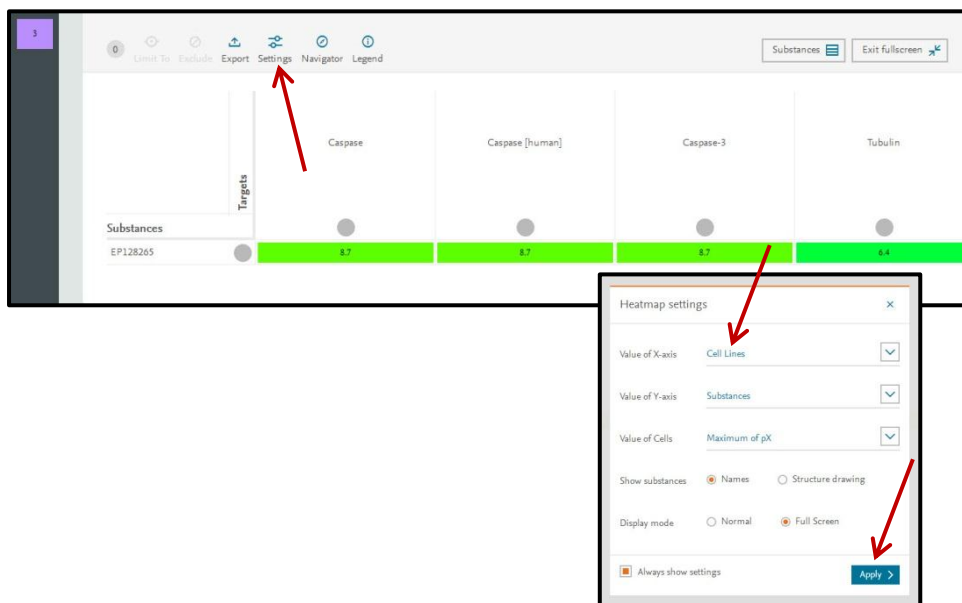
The Heatmap is displayed which provide a profile of target hits by the corresponding compound.

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

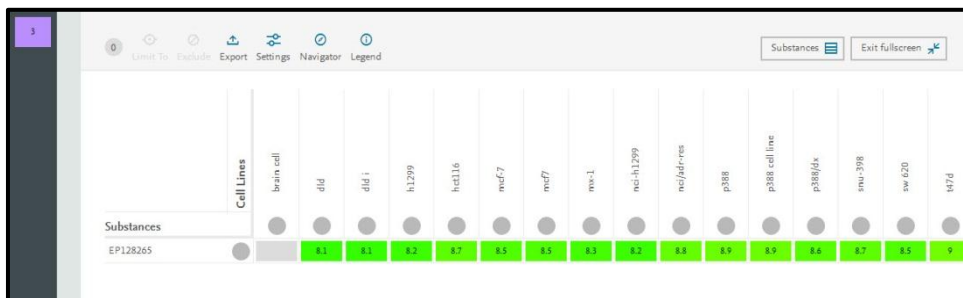
Substances	Caspase	Caspase [human]	Caspase-3	Tubulin
EP128265	8.7	8.7	8.7	8.4

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**.

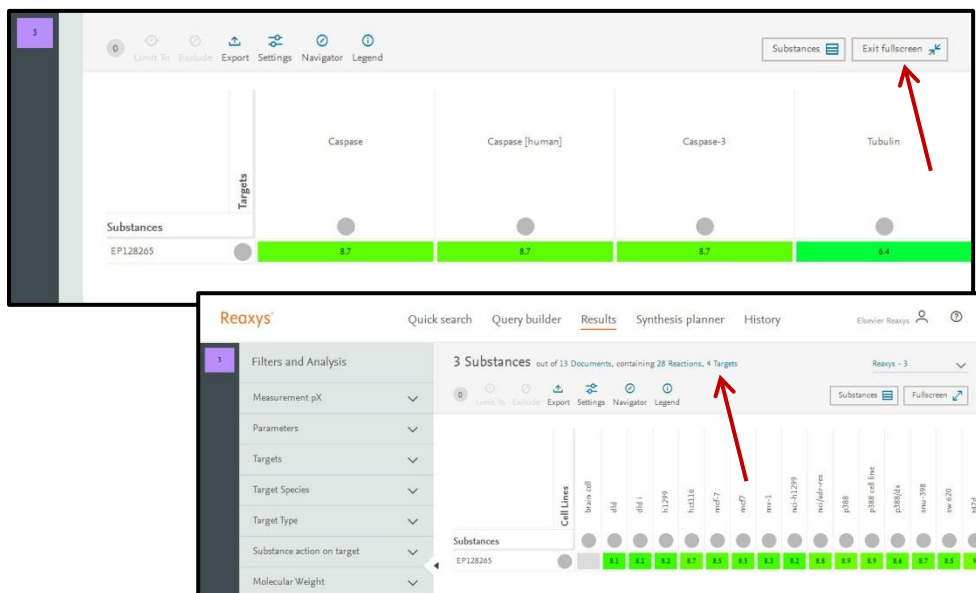


A profile on Cell lines appears in the Heatmap view.

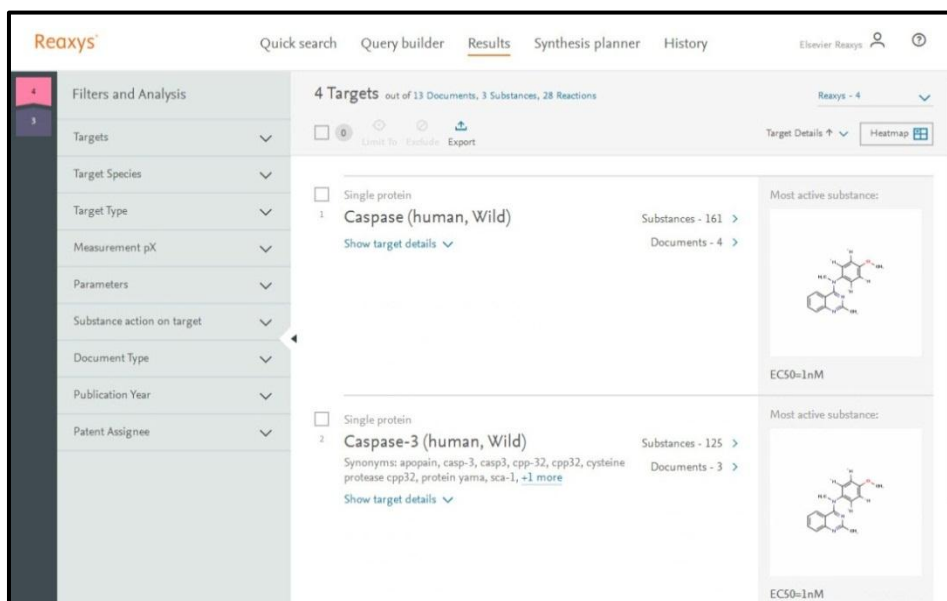


## ❖ View Target Details

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 2<sup>nd</sup> results.

The screenshot shows the Reaxys search results page. On the left is a 'Filters and Analysis' sidebar. The main content area displays '4 Targets' from 13 documents, 3 substances, and 28 reactions. The first target is 'Caspase (human, Wild)' with 161 substances and 4 documents. The second target is 'Caspase-3 (human, Wild)' with 125 substances and 3 documents. A red arrow points to the 'Show target details' link for the second target.

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).

