BioSolveIT
expect actives!

infiniSee

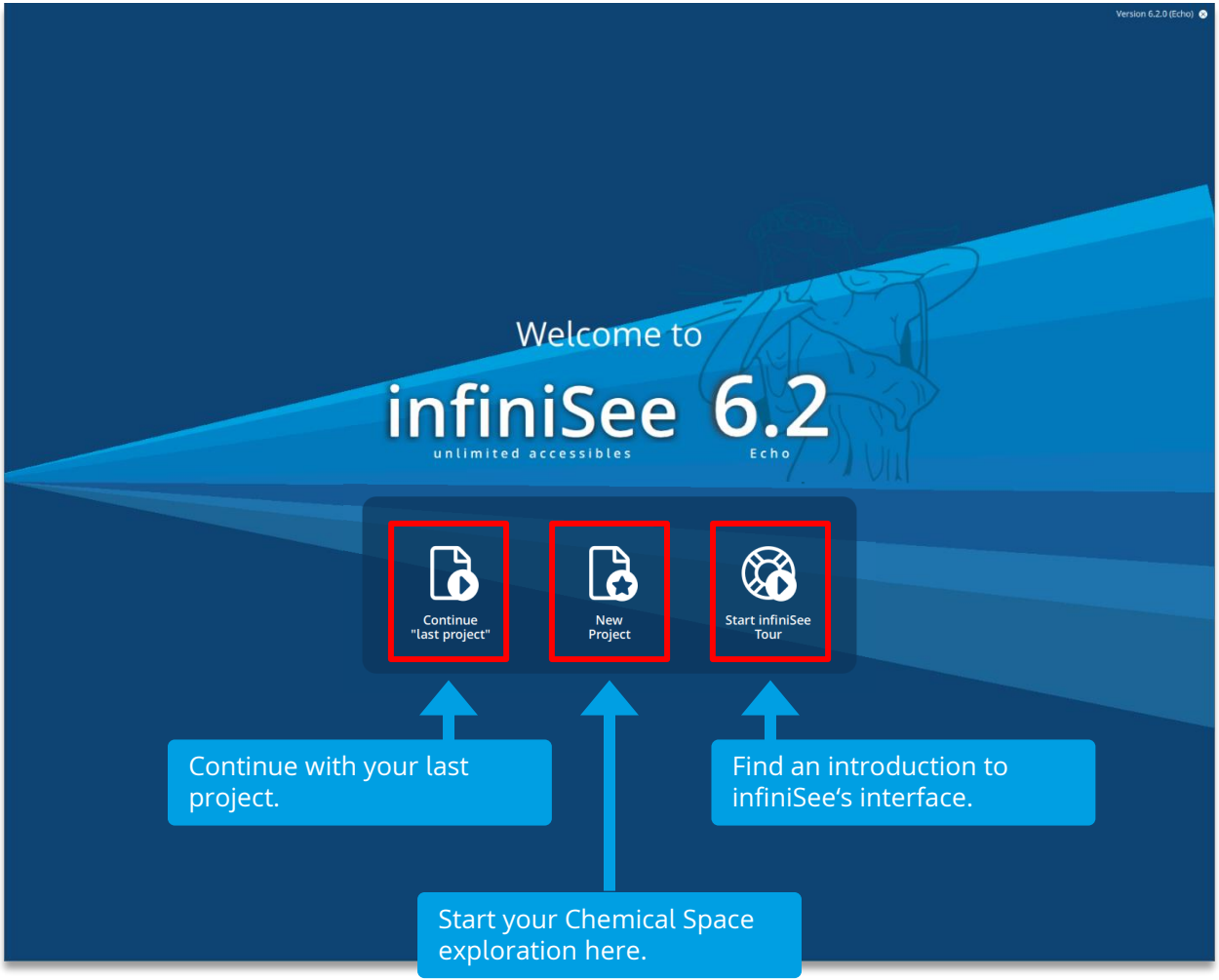
Beginner's Guide

Version 6.2 - Echo

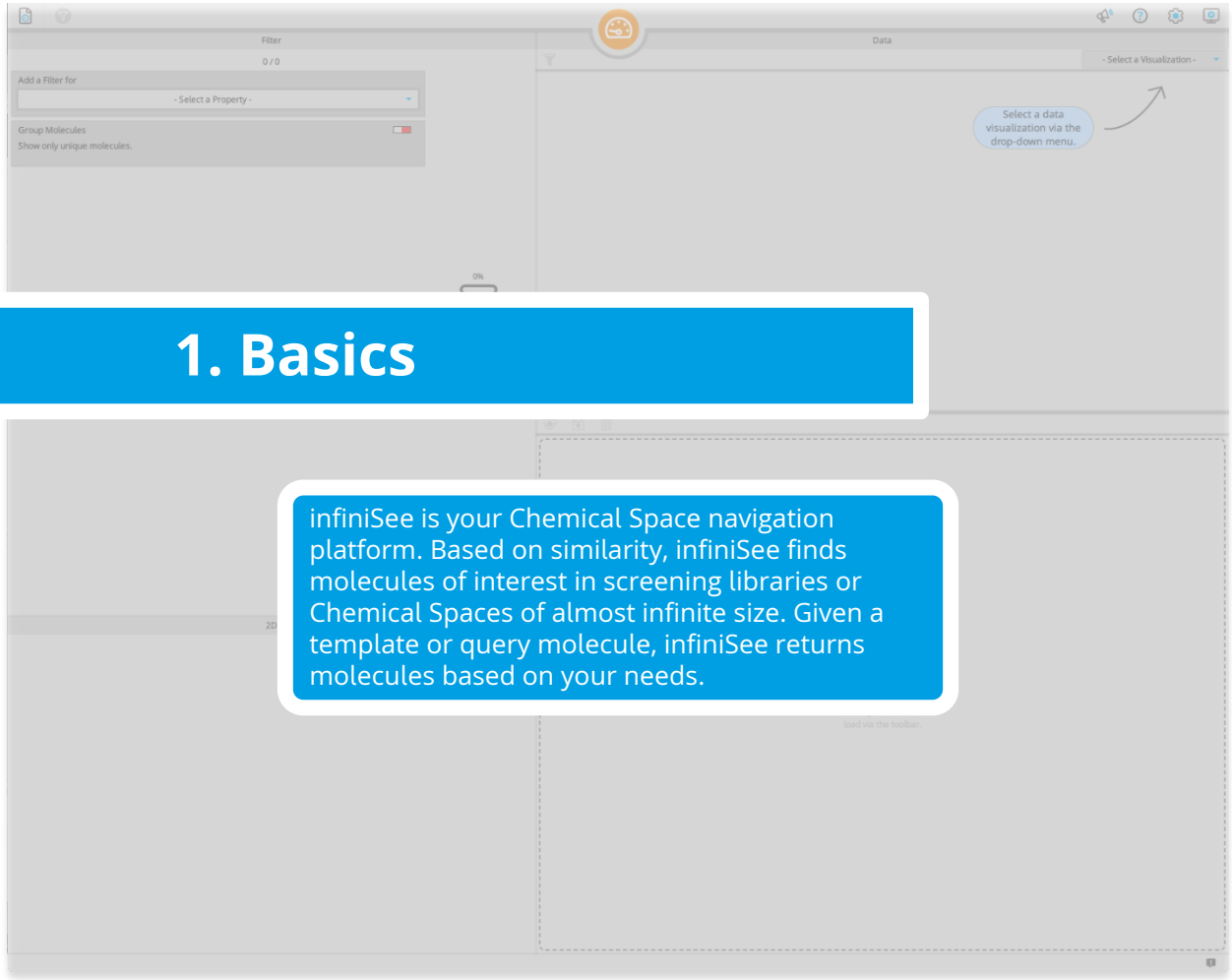
Born too late to explore the earth.
Born too early to explore the universe.
Born just in time to explore the
Chemical Space.

Content

Click on the section you are interested in

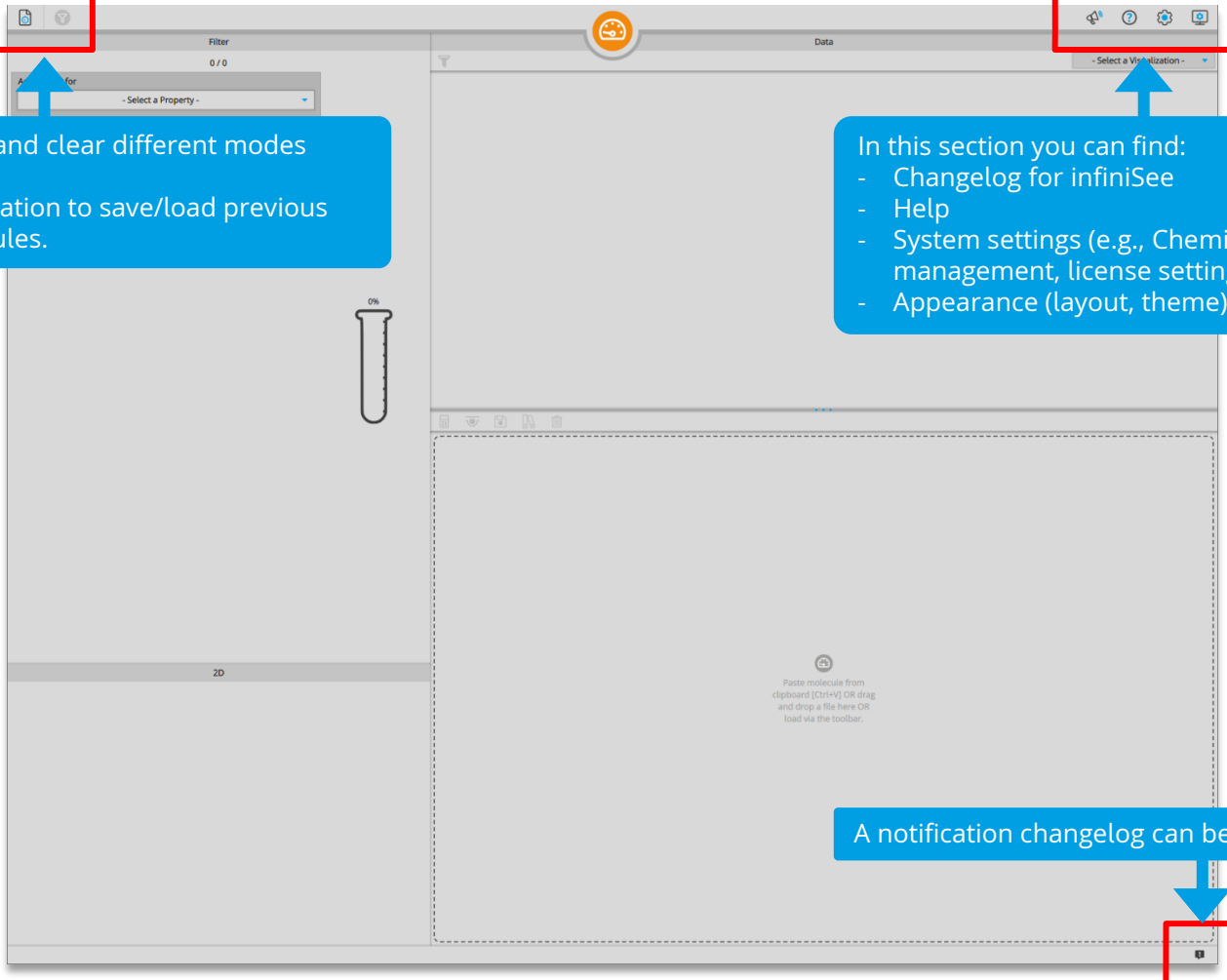

Version 6.2.0 (Echo)
Welcome to
infiniSee 6.2
unlimited accessibles
Echo
Continue "last project"
New Project
Start infiniSee Tour
Continue with your last project.
Start your Chemical Space exploration here.
Find an introduction to infiniSee's interface.


Version 6.2.0 (Echo)
Welcome to
infiniSee 6.2
unlimited accessibles
Echo
What are you trying to achieve?
Select to start a mode!
Find scaffold hops and pharmacophore matches
Retrieve structurally similar analogs
Seek for substructure motifs in hits
Load molecules for analysis
After starting a new project, infiniSee assists you in choosing the appropriate mode to accomplish your project objectives.



1. Basics

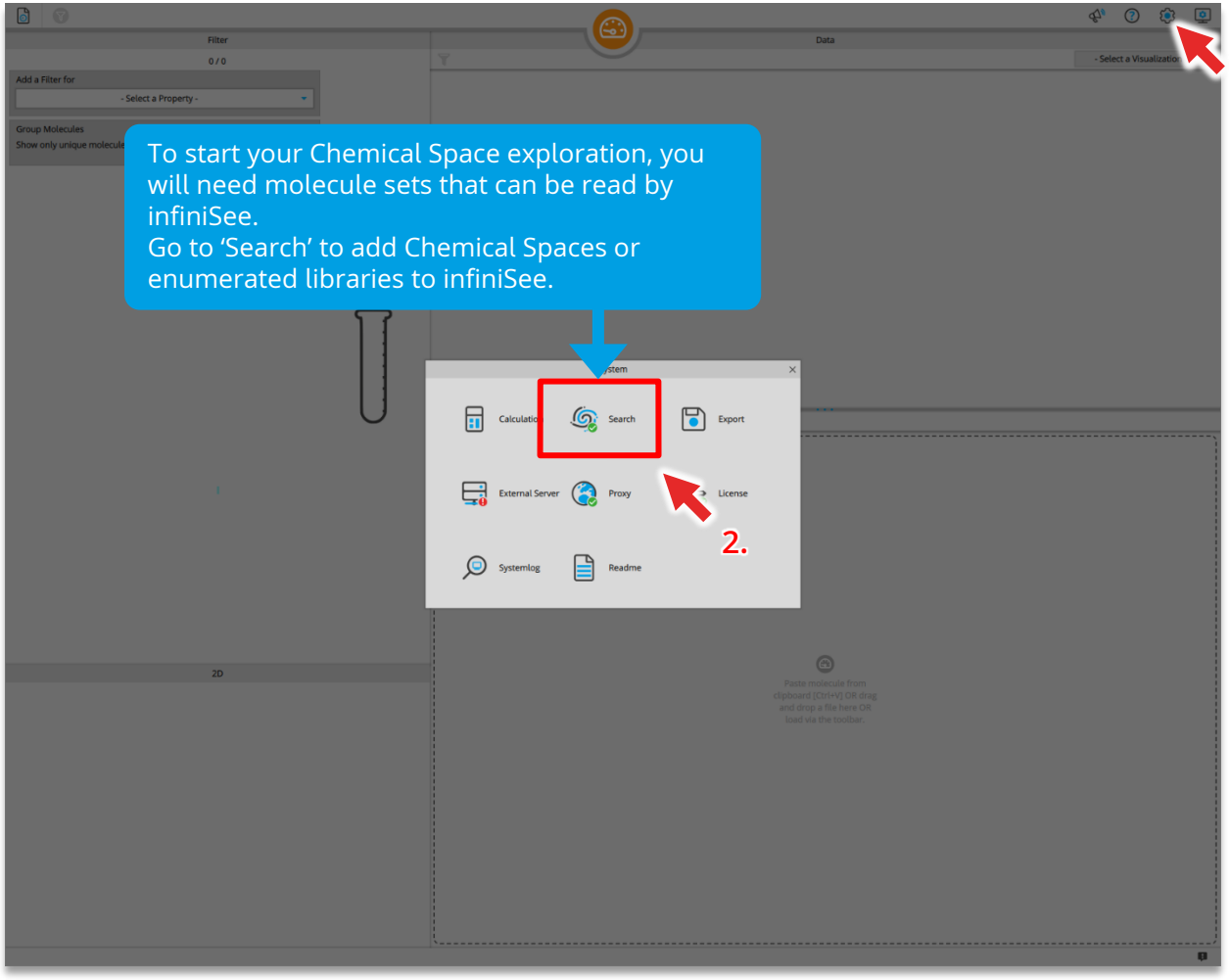
infiniSee is your Chemical Space navigation platform. Based on similarity, infiniSee finds molecules of interest in screening libraries or Chemical Spaces of almost infinite size. Given a template or query molecule, infiniSee returns molecules based on your needs.

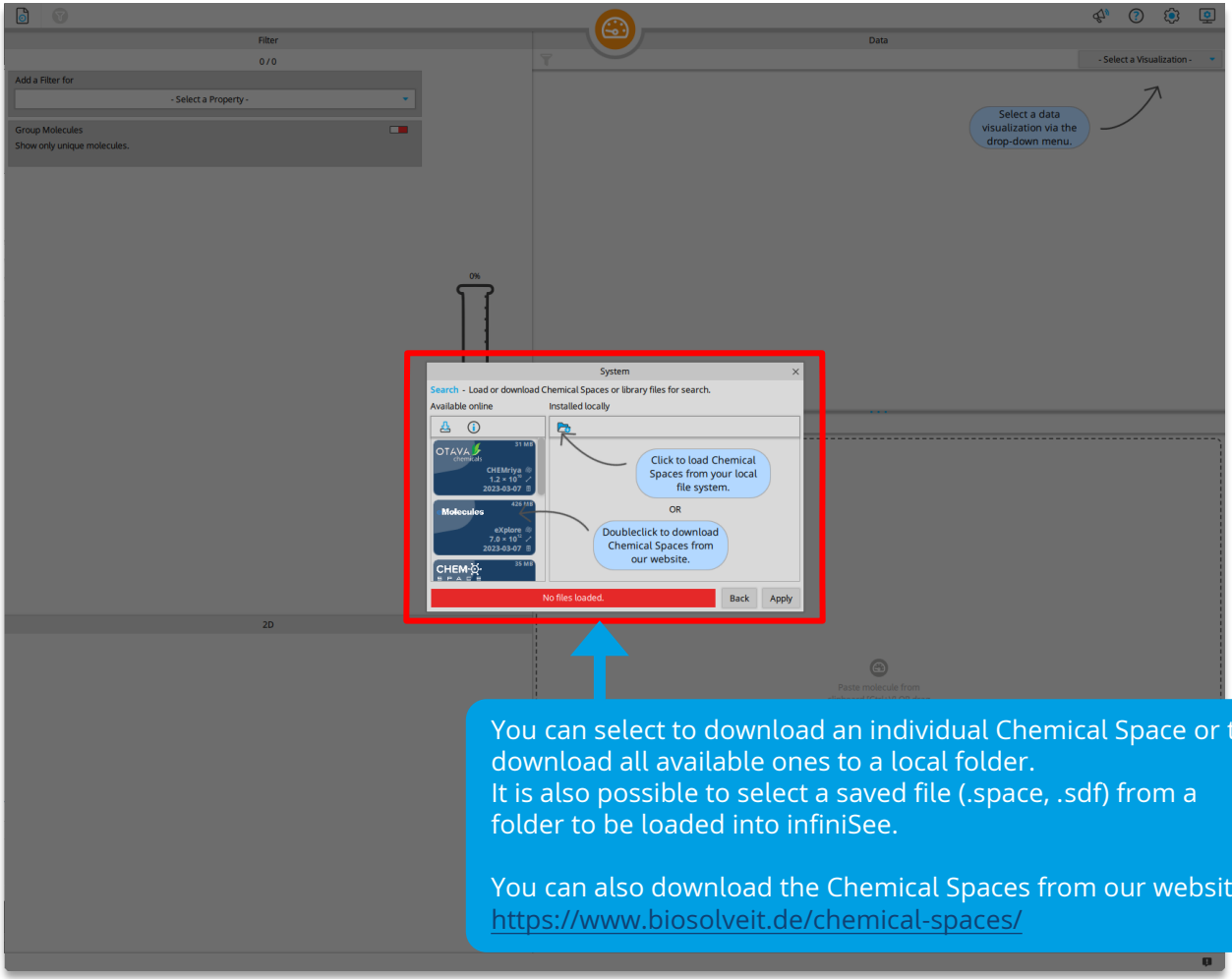


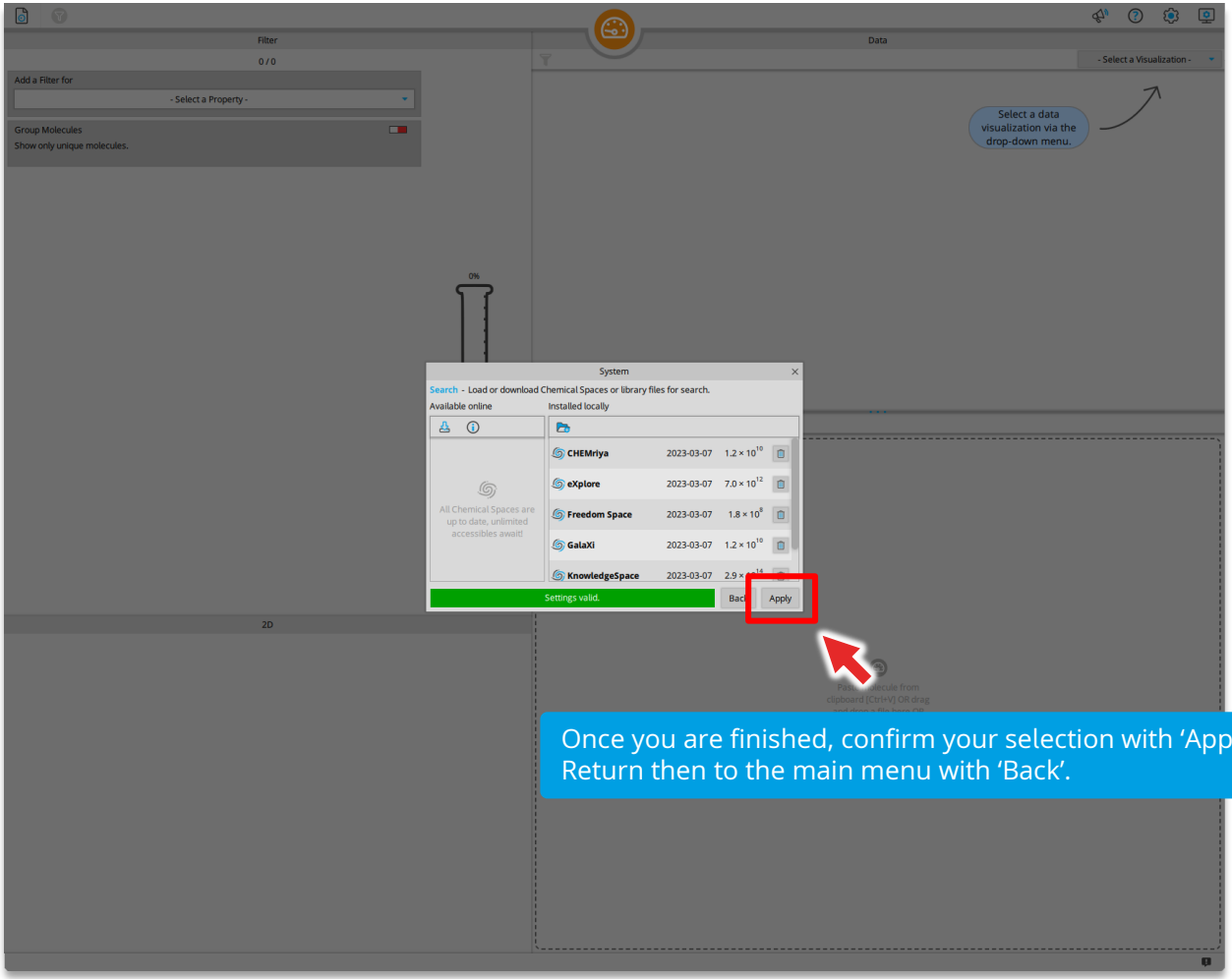
Start new project and clear different modes here.
This is also the location to save/load previous projects or molecules.

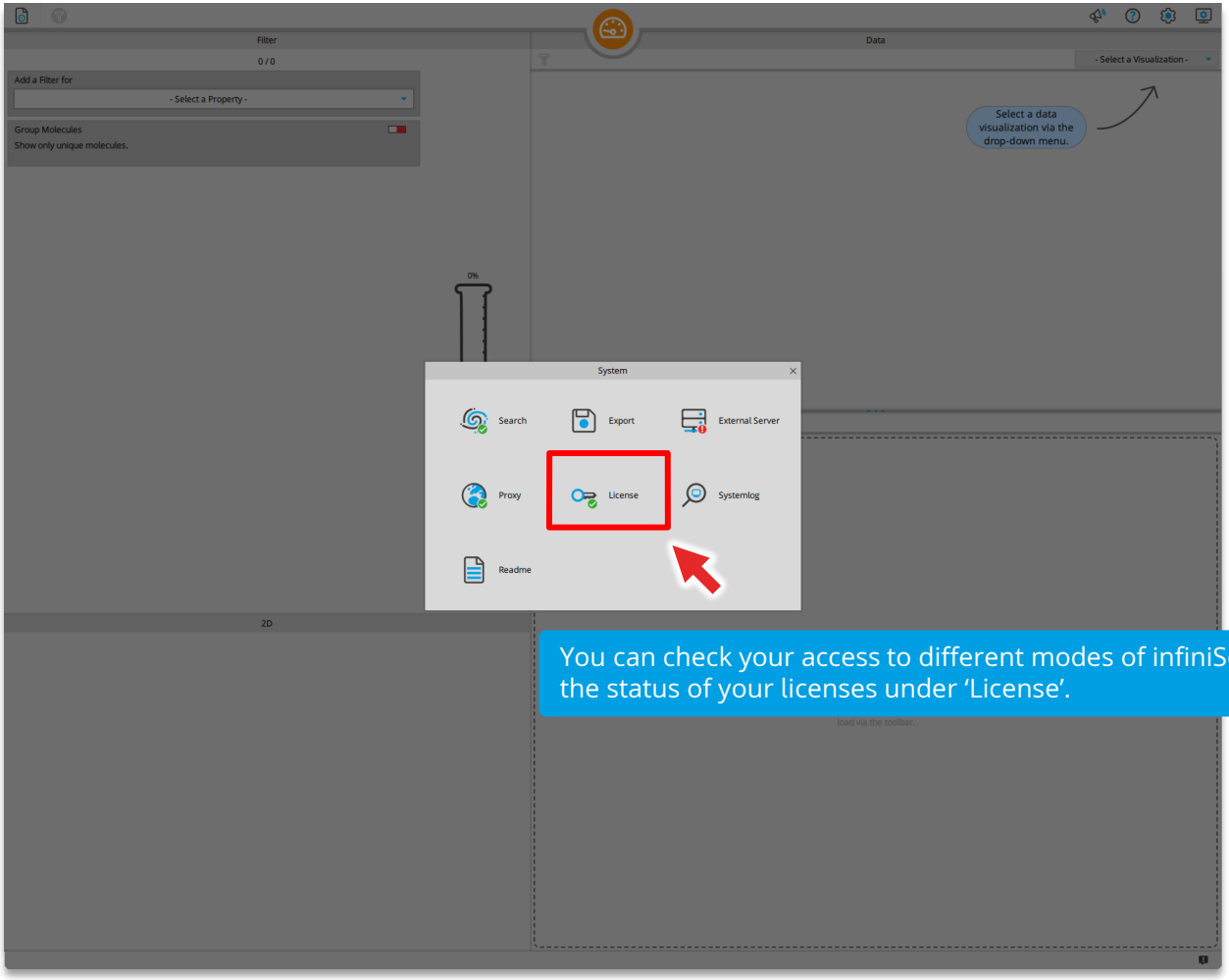
In this section you can find:
- Changelog for infiniSee
- Help
- System settings (e.g., Chemical Space management, license settings, system log, ...)
- Appearance (layout, theme)

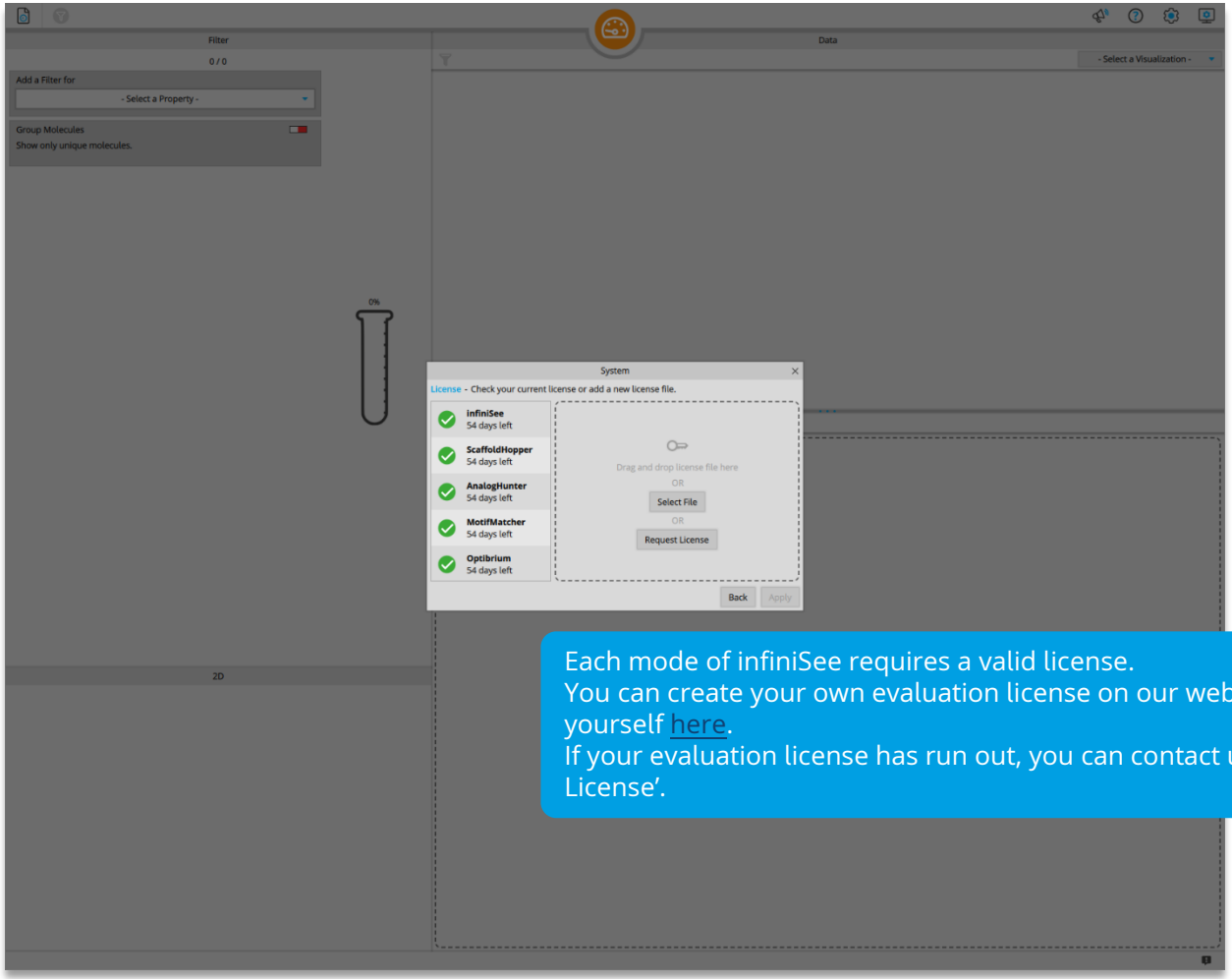
A notification changelog can be found here.


To start your Chemical Space exploration, you will need molecule sets that can be read by infiniSee.
Go to 'Search' to add Chemical Spaces or enumerated libraries to infiniSee.
1.
2.
Search
Export
External Server
Proxy
License
Systemlog
Readme


Filter
0 / 0
Add a Filter for
- Select a Property -
Group Molecules
Show only unique molecules.
Data
- Select a Visualization -
Select a data visualization via the drop-down menu.
0%
System
Search - Load or download Chemical Spaces or library files for search.
Available online
Installed locally
Click to load Chemical Spaces from your local file system.
OR
Doubleclick to download Chemical Spaces from our website.
No files loaded.
Back
Apply
2D
Paste molecule from
You can select to download an individual Chemical Space or to download all available ones to a local folder.
It is also possible to select a saved file (.space, .sdf) from a folder to be loaded into infiniSee.
You can also download the Chemical Spaces from our website:
https://www.biosolveit.de/chemical-spaces/

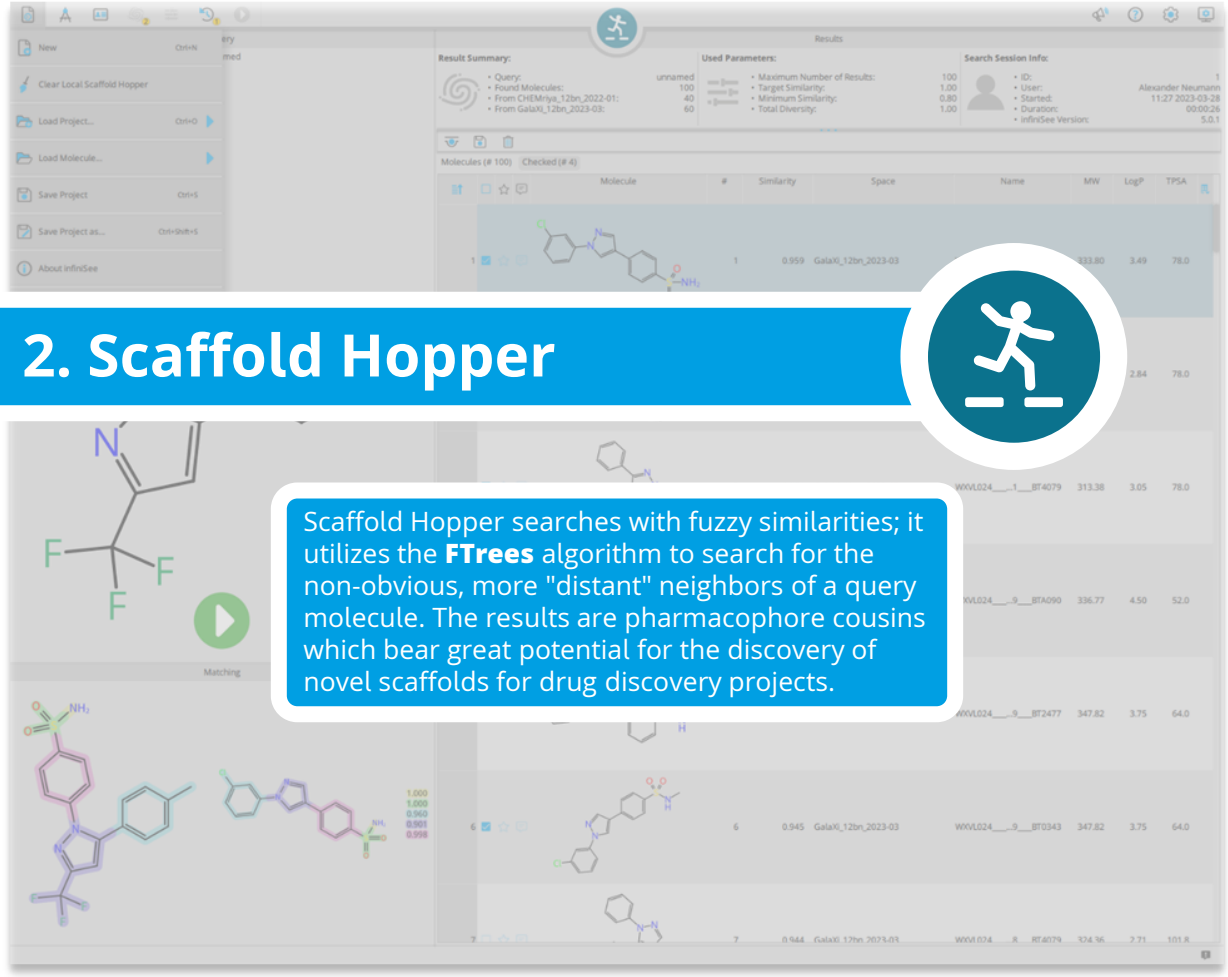

Filter
0 / 0
Add a Filter for
- Select a Property -
Group Molecules
Show only unique molecules.
Data
- Select a Visualization -
Select a data visualization via the drop-down menu.
0%
System
Search - Load or download Chemical Spaces or library files for search.
Available online
Installed locally
All Chemical Spaces are up to date, unlimited accessibles await!
CHEMriya 2023-03-07 1.2 × 10^10
eXplore 2023-03-07 7.0 × 10^12
Freedom Space 2023-03-07 1.8 × 10^8
GalaXi 2023-03-07 1.2 × 10^10
KnowledgeSpace 2023-03-07
Settings valid.
Back
Apply
2D
Once you are finished, confirm your selection with ‘Apply’.
Return then to the main menu with ‘Back’.


Filter
0 / 0
Add a Filter for
- Select a Property -
Group Molecules
Show only unique molecules.
Data
- Select a Visualization -
Select a data visualization via the drop-down menu.
0%
System
Search
Export
External Server
Proxy
License
Systemlog
Readme
2D
You can check your access to different modes of infiniSee as well as the status of your licenses under ‘License’.

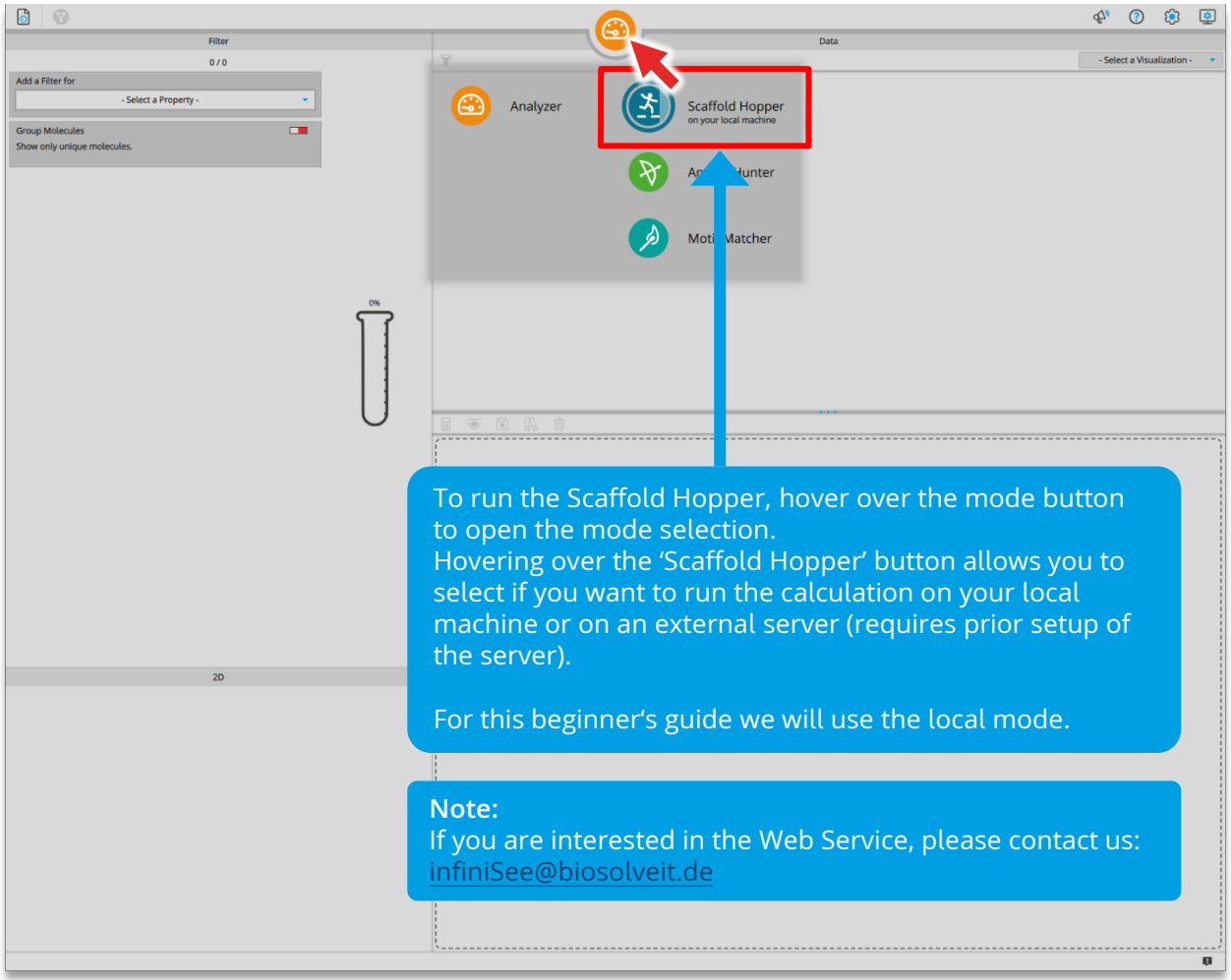


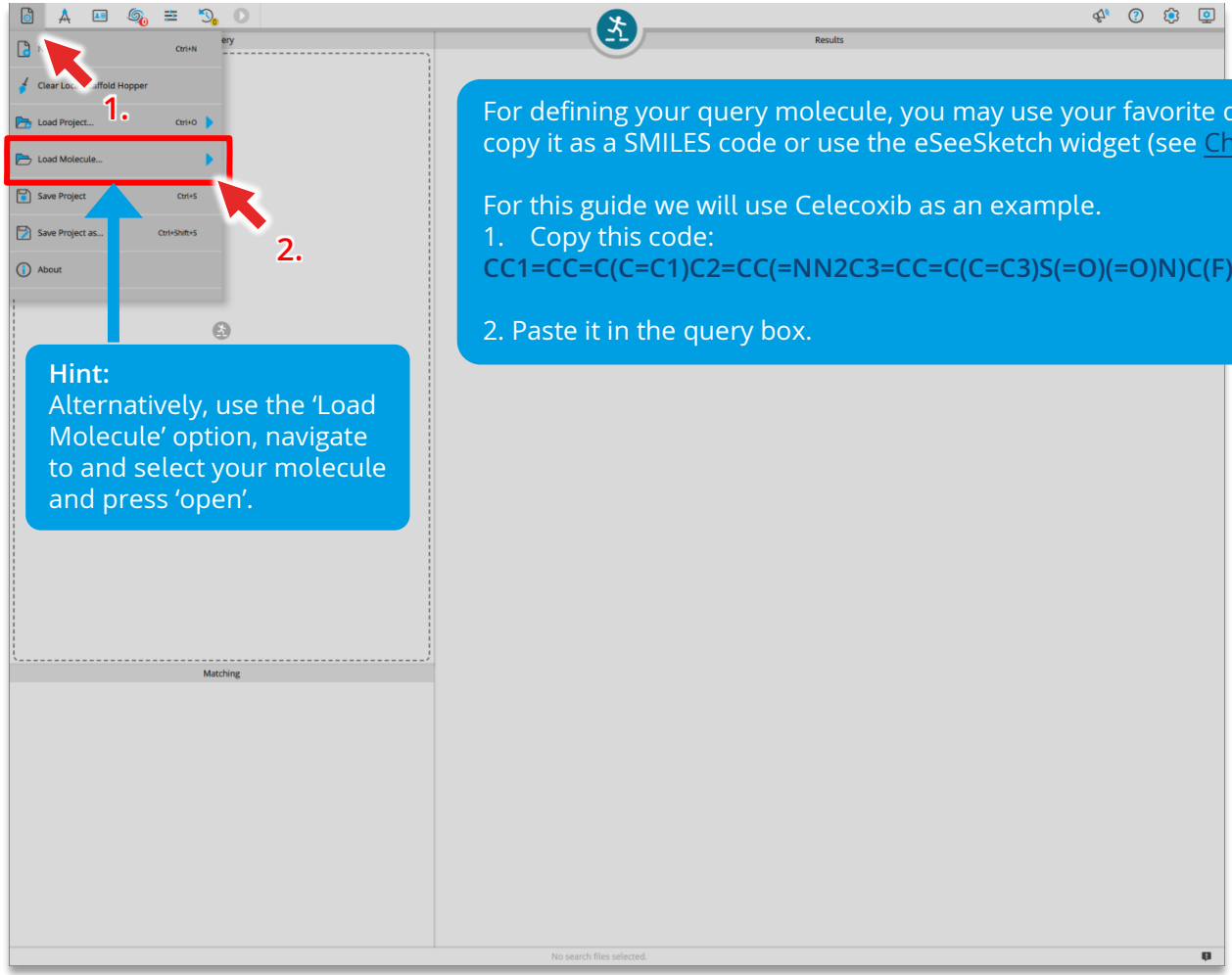
Each mode of infiniSee requires a valid license.
You can create your own evaluation license on our website by yourself here.
If your evaluation license has run out, you can contact us via 'Request License'.

2. Scaffold Hopper



Scaffold Hopper searches with fuzzy similarities; it utilizes the **FTrees** algorithm to search for the non-obvious, more "distant" neighbors of a query molecule. The results are pharmacophore cousins which bear great potential for the discovery of novel scaffolds for drug discovery projects.


Filter
0 / 0
Add a Filter for
- Select a Property -
Group Molecules
Show only unique molecules.
Data
- Select a Visualization -
Analyzer
Scaffold Hopper
on your local machine
Matcher
0%
2D
To run the Scaffold Hopper, hover over the mode button to open the mode selection.
Hovering over the 'Scaffold Hopper' button allows you to select if you want to run the calculation on your local machine or on an external server (requires prior setup of the server).
For this beginner's guide we will use the local mode.
Note:
If you are interested in the Web Service, please contact us:
infiniSee@biosolveit.de



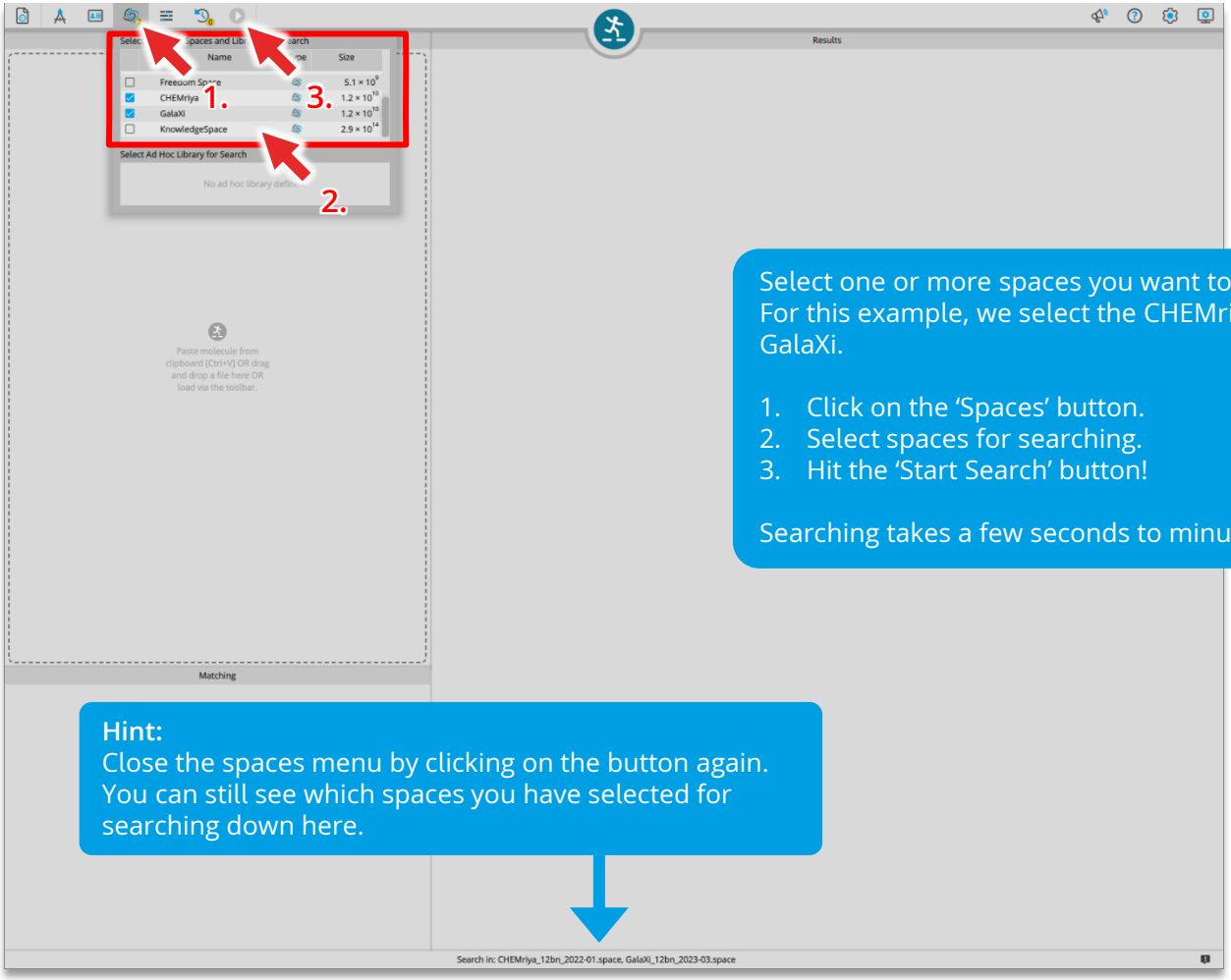
Hint:
Alternatively, use the 'Load Molecule' option, navigate to and select your molecule and press 'open'.

For defining your query molecule, you may use your favorite drawing tool and copy it as a SMILES code or use the eSeeSketch widget (see Chapter 6).

For this guide we will use Celecoxib as an example.

1. Copy this code:
CC1=CC=C(C=C1)C2=CC(=NN2C3=CC=C(C=C3)S(=O)(=O)N)C(F)(F)F

2. Paste it in the query box.

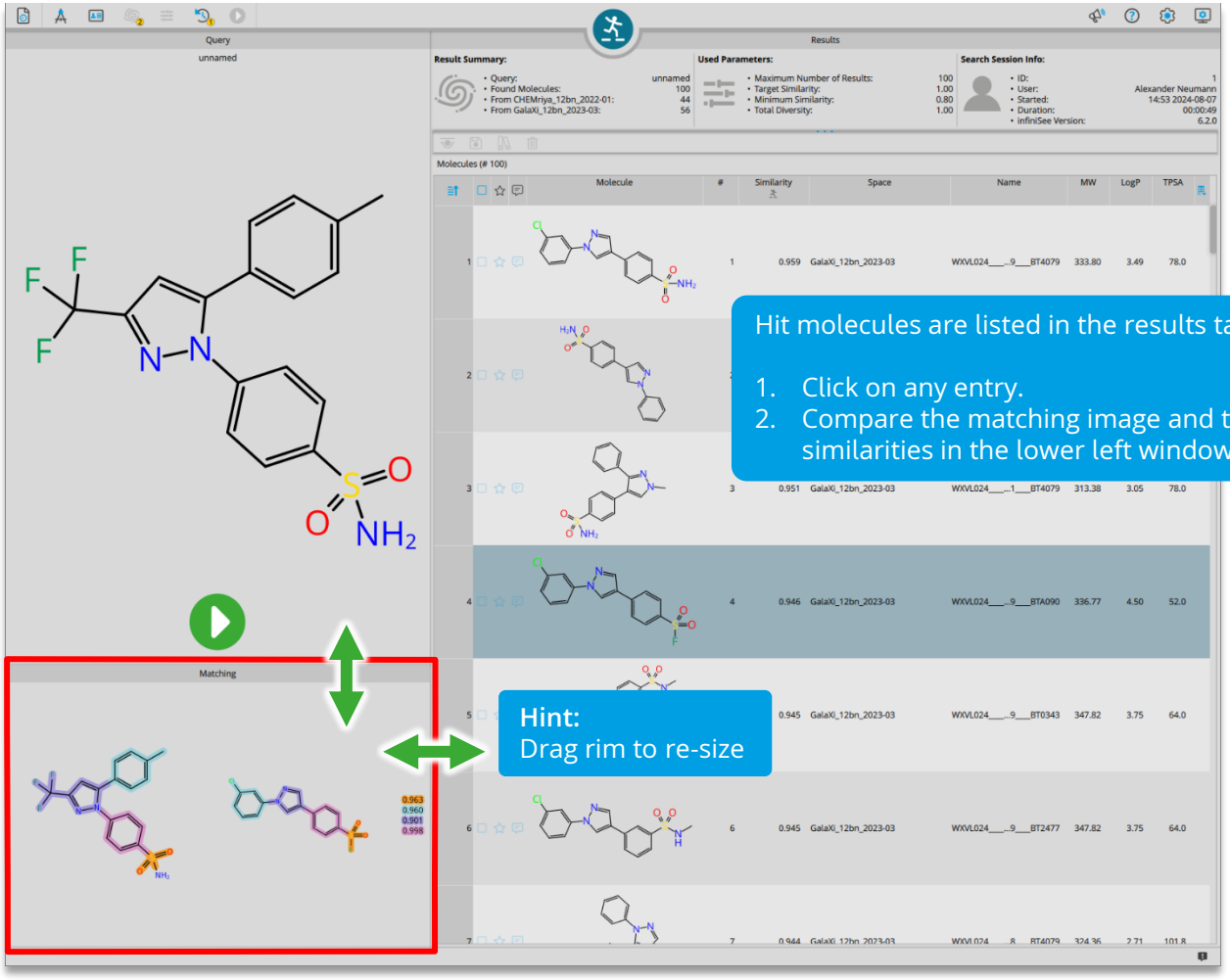


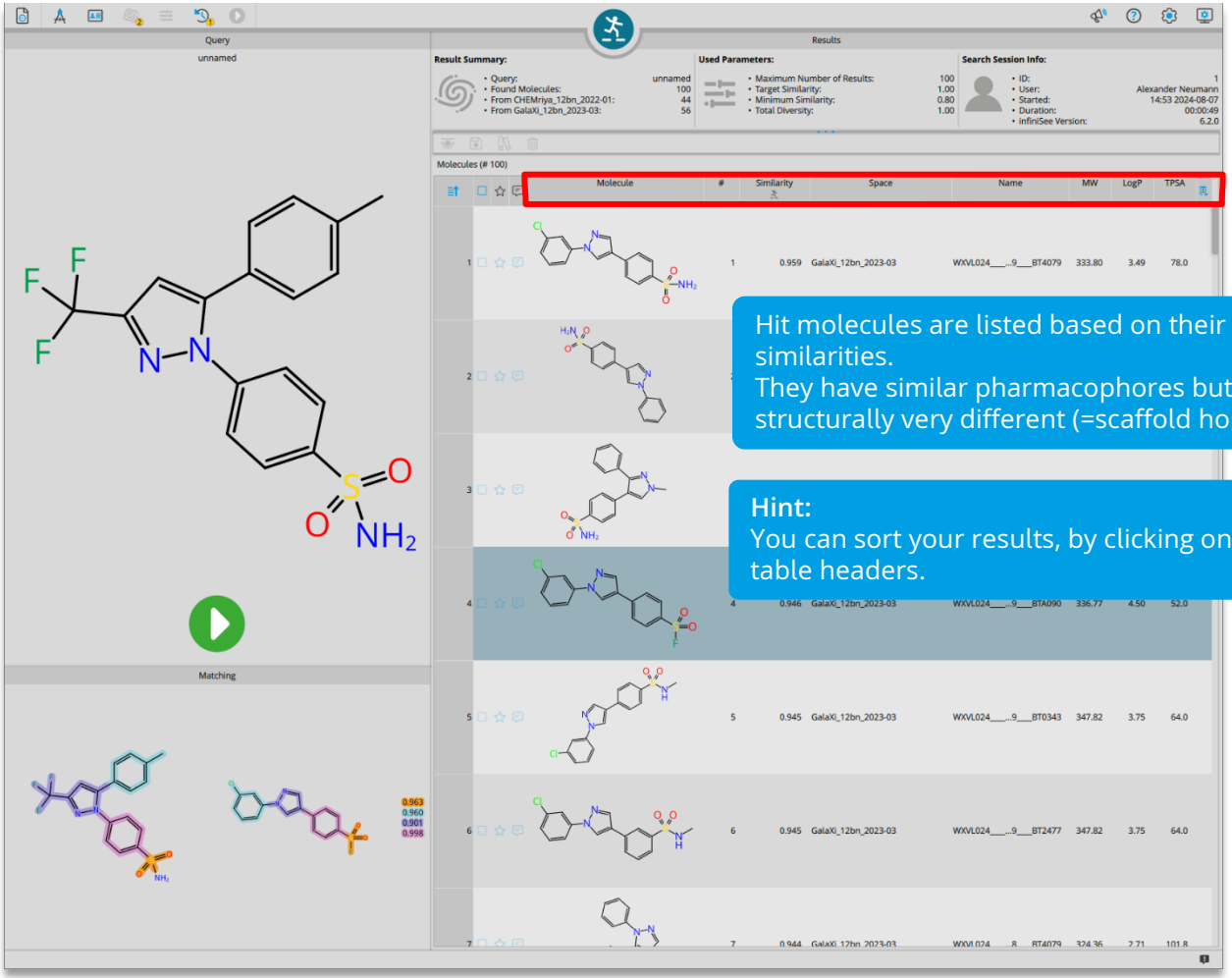
Select one or more spaces you want to search in. For this example, we select the CHEMriya and GalaXi.

1. Click on the ‘Spaces’ button.
2. Select spaces for searching.
3. Hit the ‘Start Search’ button!

Searching takes a few seconds to minutes...

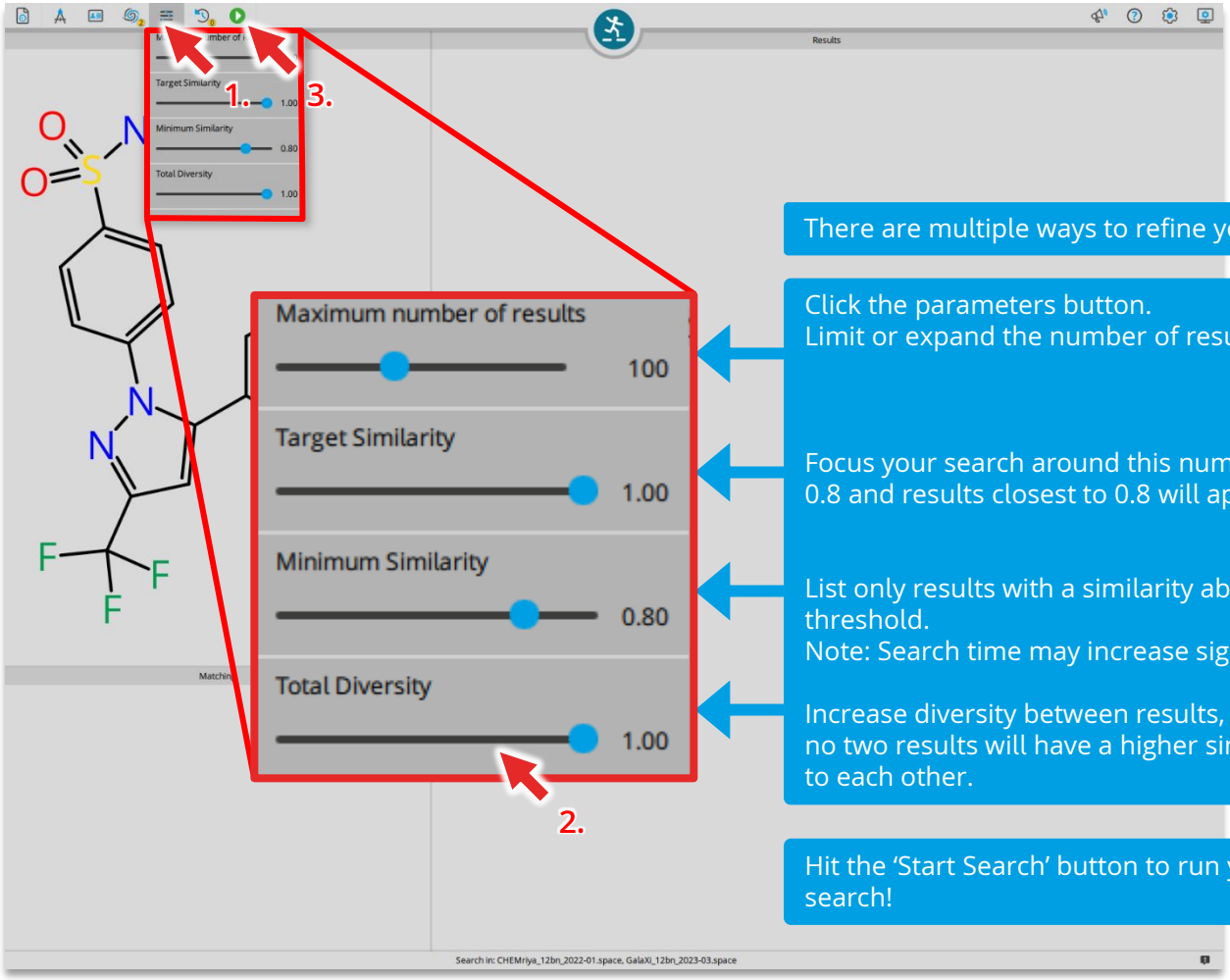
Hint:
Close the spaces menu by clicking on the button again. You can still see which spaces you have selected for searching down here.


Query
unnamed
Results
Result Summary:
Query: unnamed
Found Molecules: 100
From CHEMriya_12bn_2022-01: 44
From GalaXi_12bn_2023-03: 56
Used Parameters:
Maximum Number of Results: 100
Target Similarity: 1.00
Minimum Similarity: 0.80
Total Diversity: 1.00
Search Session Info:
ID: 1
User: Alexander Neumann
Started: 14:53 2024-08-07
Duration: 00:00:49
InfiniSee Version: 6.2.0
Molecules (# 100)
Molecule
#
Similarity
Space
Name
MW
LogP
TPSA
Matching
0.963
0.960
0.901
0.998
Hit molecules are listed in the results table.
1. Click on any entry.
2. Compare the matching image and the local similarities in the lower left window.
Hint:
Drag rim to re-size



Hit molecules are listed based on their FTrees-similarities.
They have similar pharmacophores but can be structurally very different (=scaffold hopping).

Hint:
You can sort your results, by clicking on any of the table headers.



There are multiple ways to refine your searches.

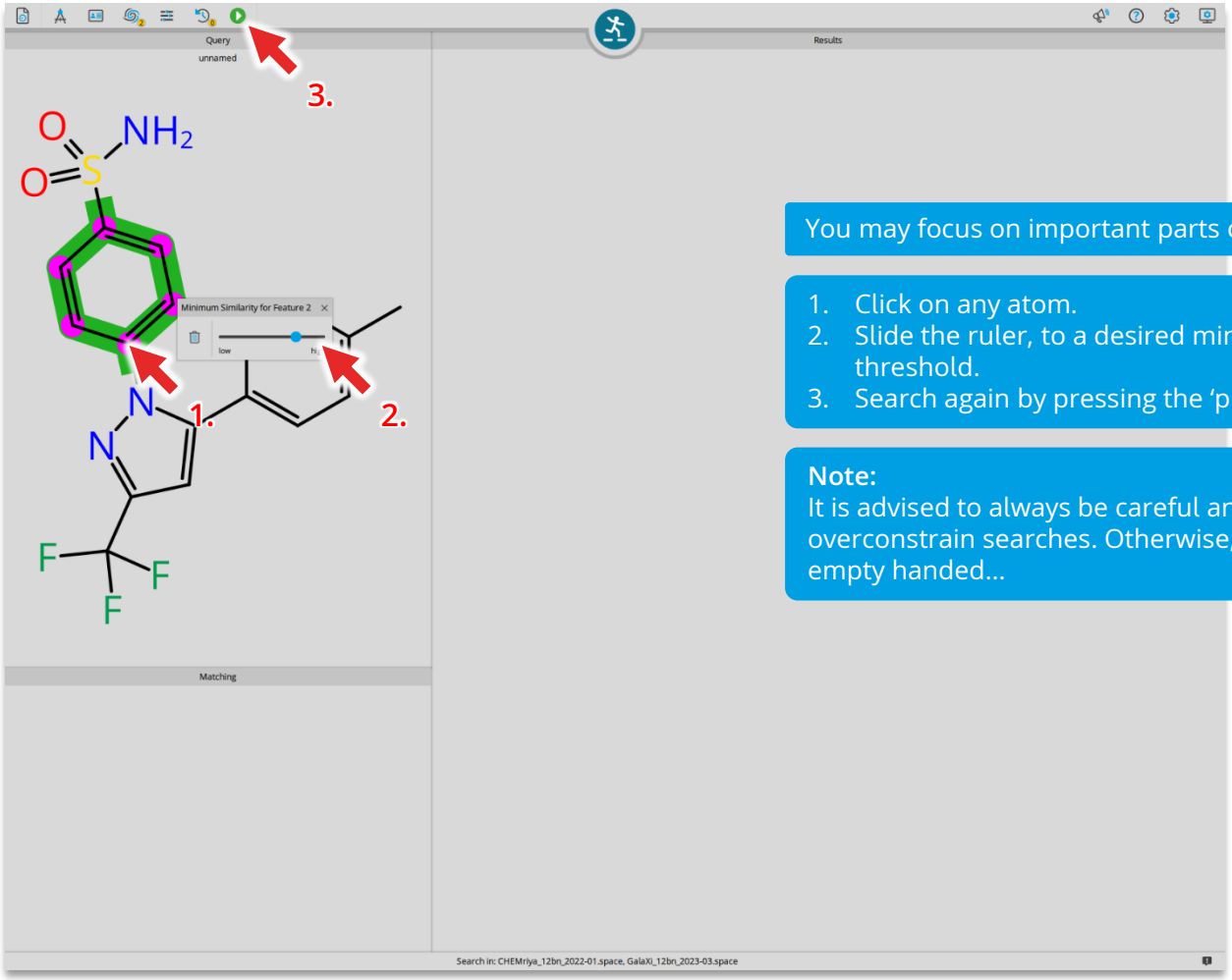
Click the parameters button.
Limit or expand the number of results.

Focus your search around this number, e.g., set it at 0.8 and results closest to 0.8 will appear first.

List only results with a similarity above this threshold.
Note: Search time may increase significantly!!

Increase diversity between results, e.g. if set at 0.9, no two results will have a higher similarity than 0.9 to each other.

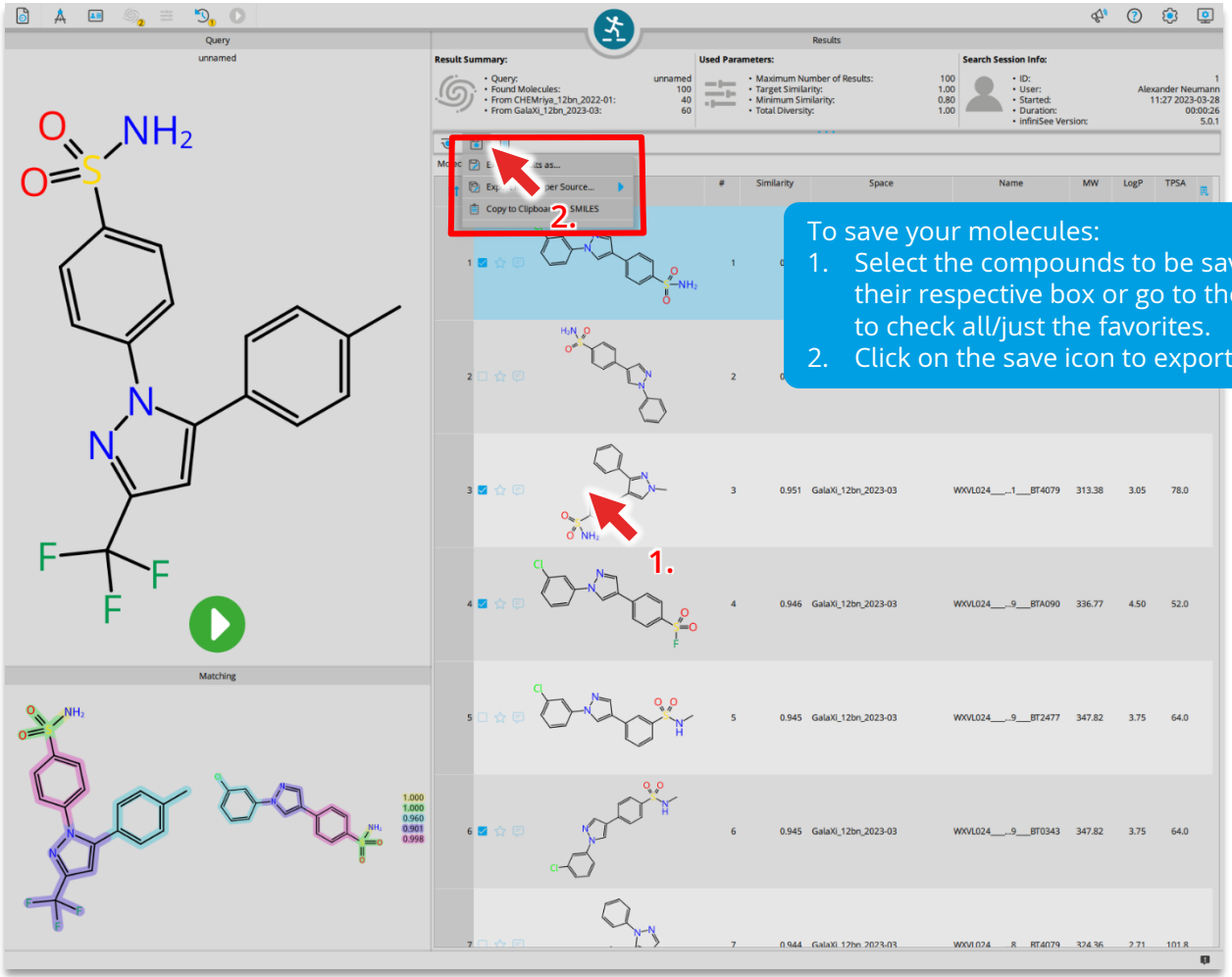
Hit the 'Start Search' button to run your refined search!

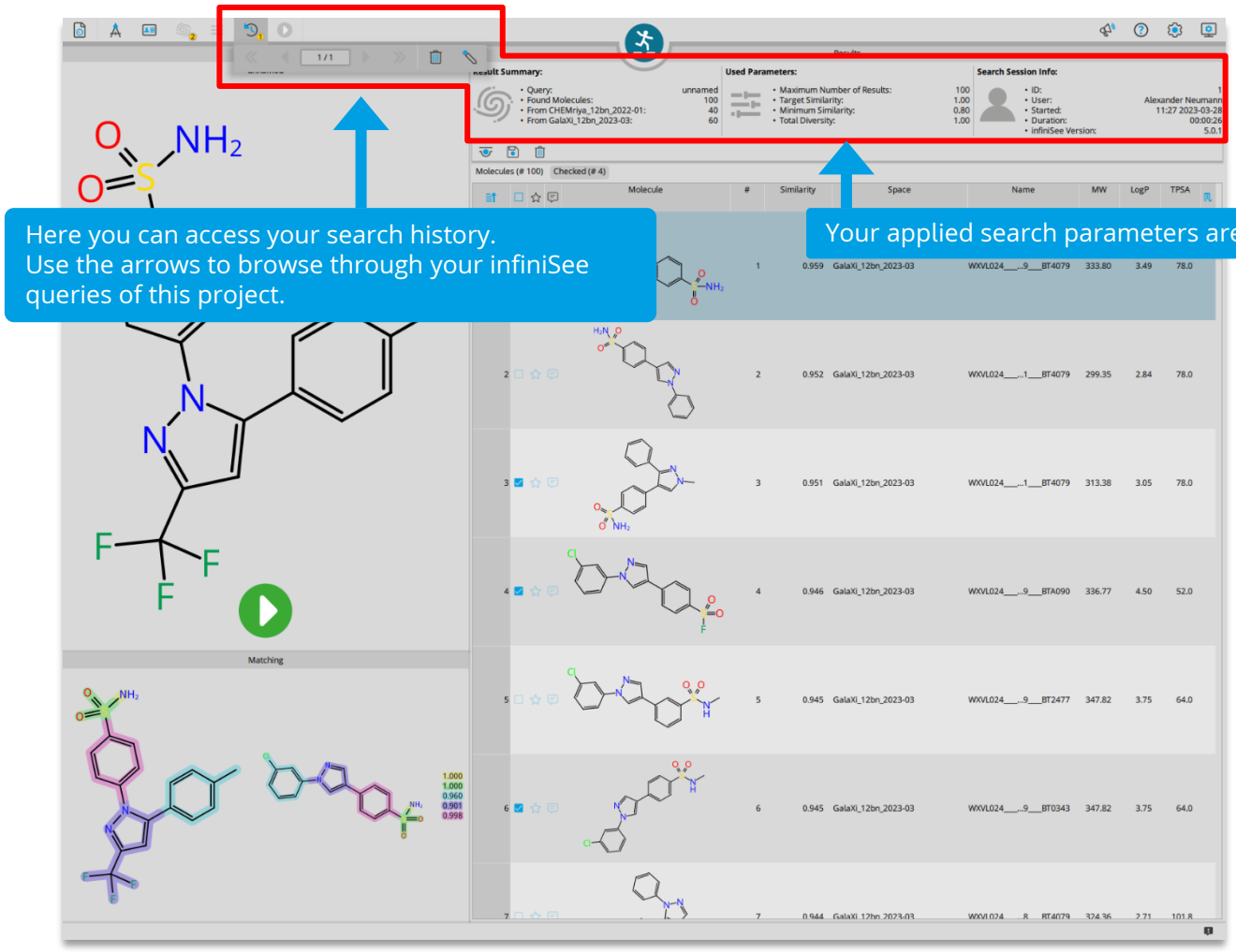


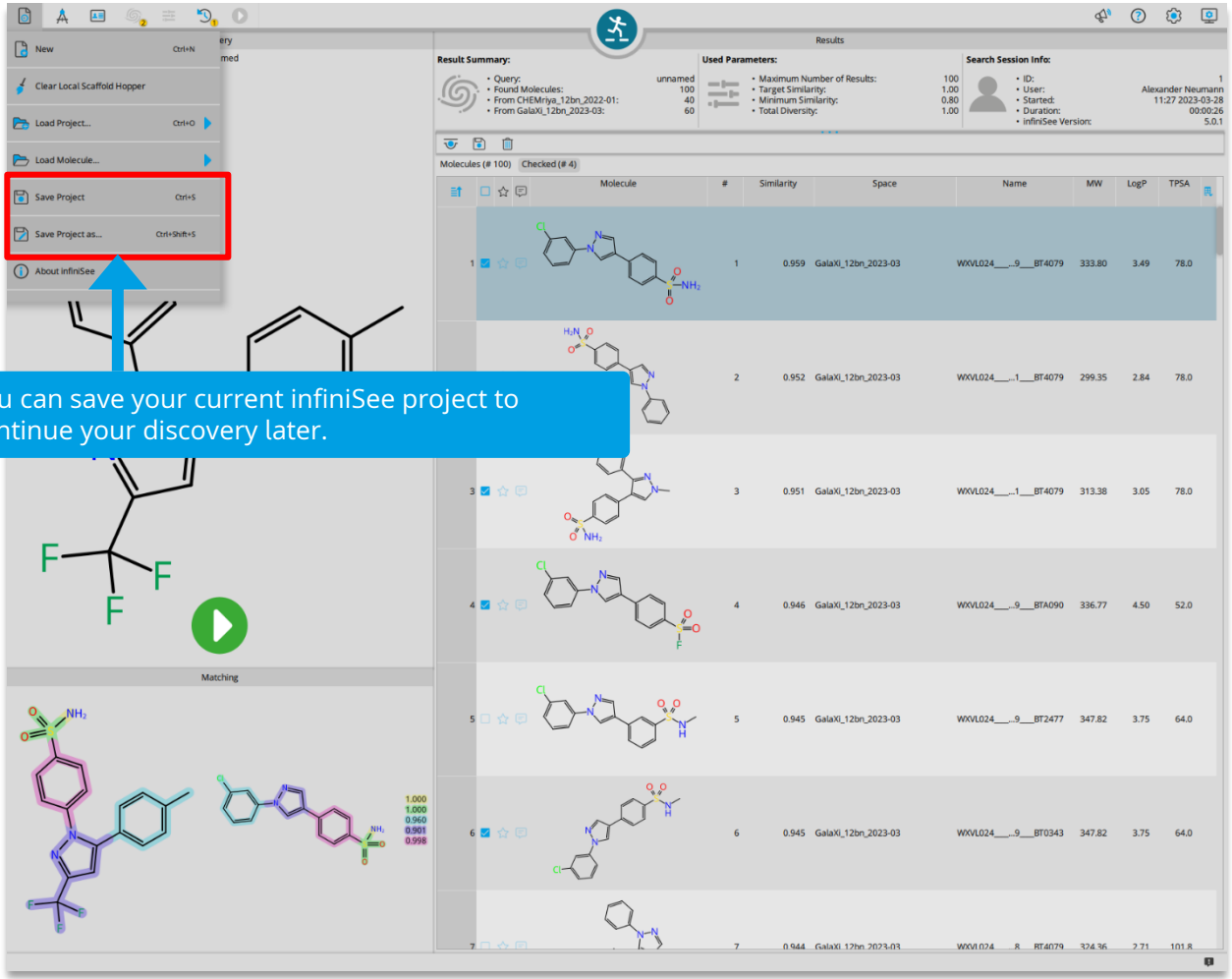
You may focus on important parts of your query.

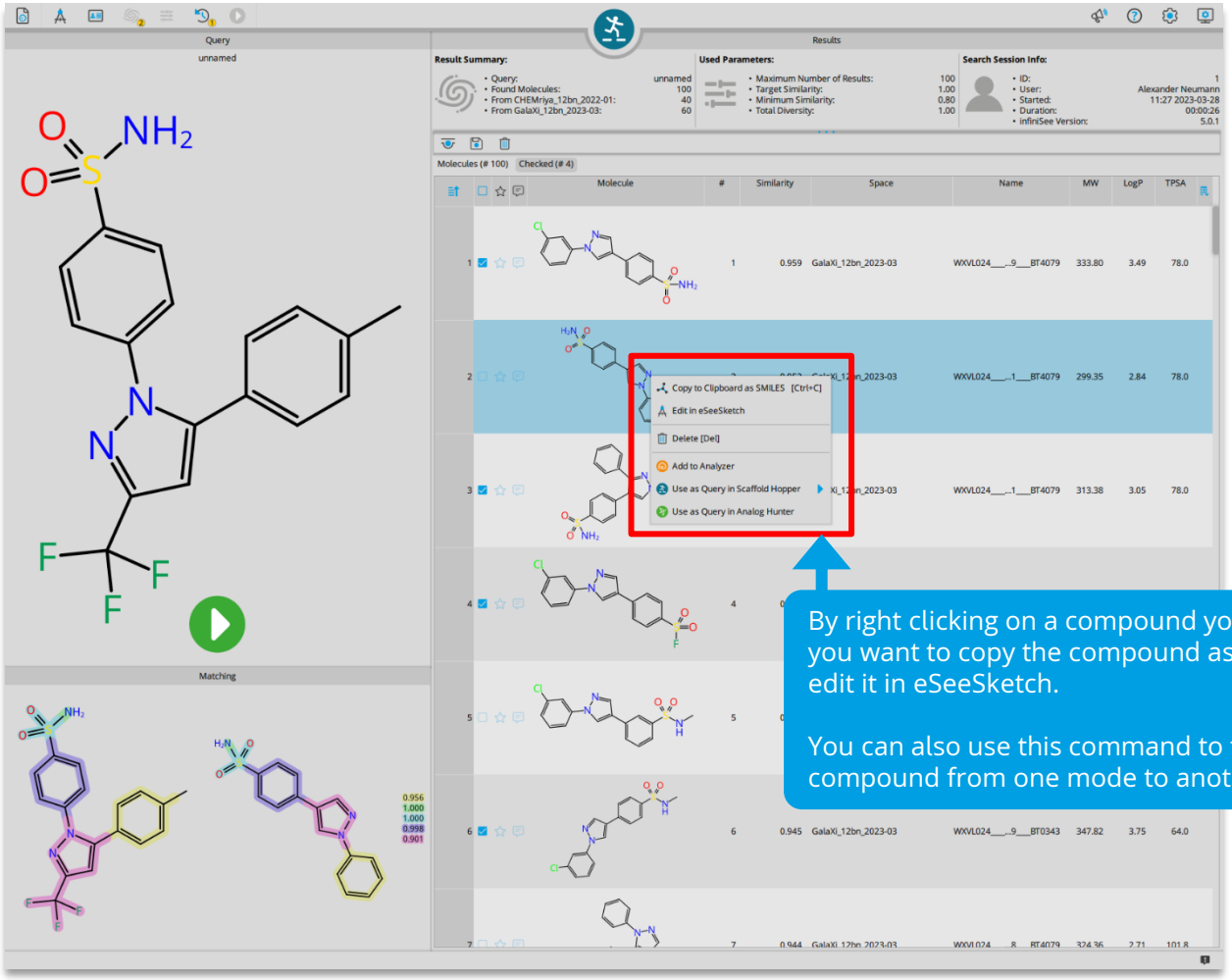
1. Click on any atom.
2. Slide the ruler, to a desired minimum similarity threshold.
3. Search again by pressing the ‘play’ button.

Note:
It is advised to always be careful and not to overconstrain searches. Otherwise, you may end up empty handed…


Query
unnamed
Matching
Results
Result Summary:
Used Parameters:
Search Session Info:
Copy to Clipboard SMILES
2.
1.
To save your molecules:
1. Select the compounds to be saved by checking their respective box or go to the top check box to check all/just the favorites.
2. Click on the save icon to export your results.

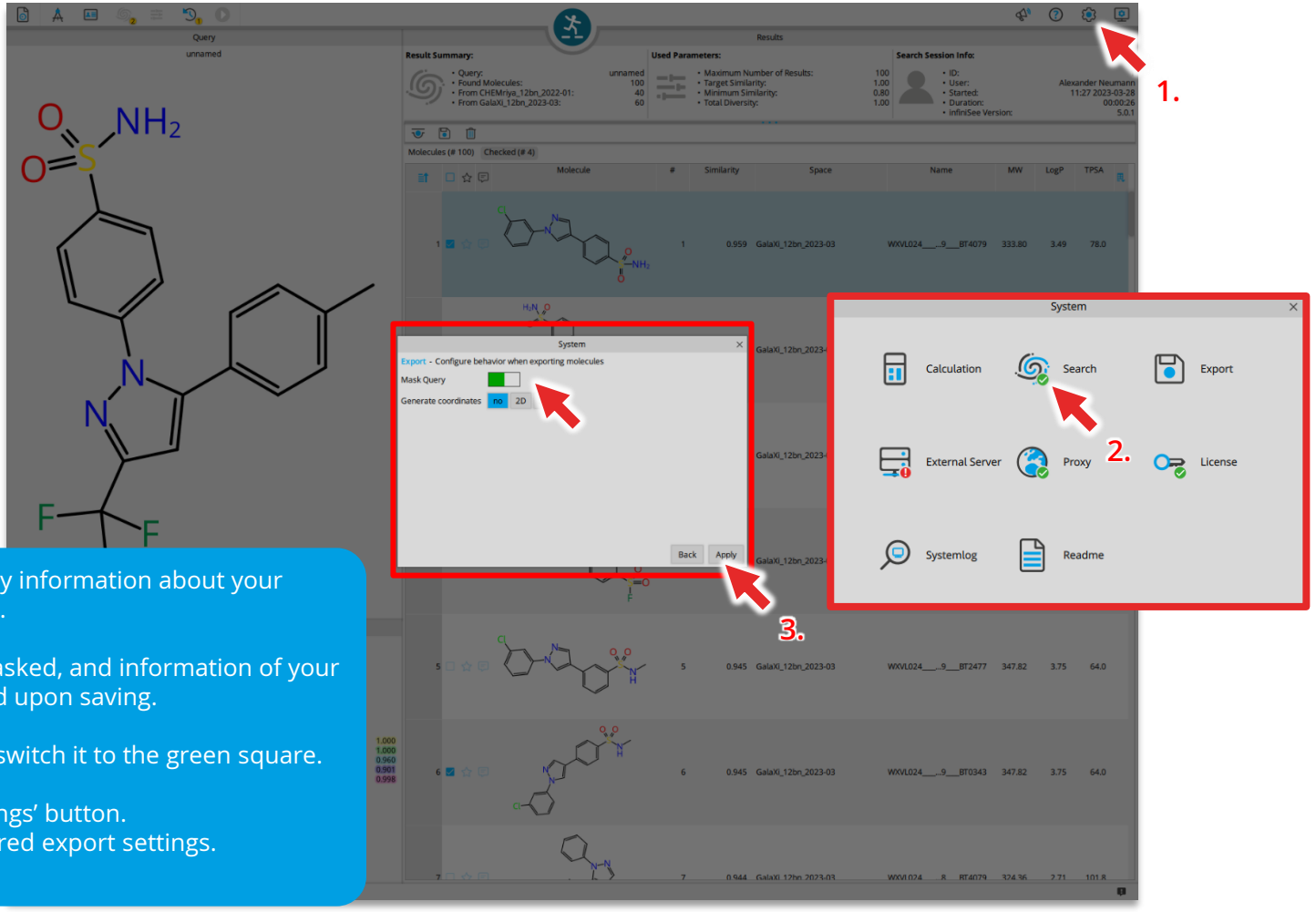

Here you can access your search history.
Use the arrows to browse through your infiniSee queries of this project.
Your applied search parameters are presented here.
Result Summary:
Used Parameters:
Search Session Info:
Molecules (# 100)
Checked (# 4)
Molecule
Similarity
Space
Name
MW
LogP
TPSA
Matching


New Ctrl+N
Clear Local Scaffold Hopper
Load Project... Ctrl+O
Load Molecule...
Save Project Ctrl+S
Save Project as... Ctrl+Shift+S
About infiniSee
You can save your current infiniSee project to continue your discovery later.
Matching
Results
Result Summary:
Used Parameters:
Search Session Info:
Molecules (# 100)
Checked (# 4)
Molecule
Similarity
Space
Name
MW
LogP
TPSA



By right clicking on a compound you can select if you want to copy the compound as SMILES or to edit it in eSeeSketch.

You can also use this command to transfer a compound from one mode to another.

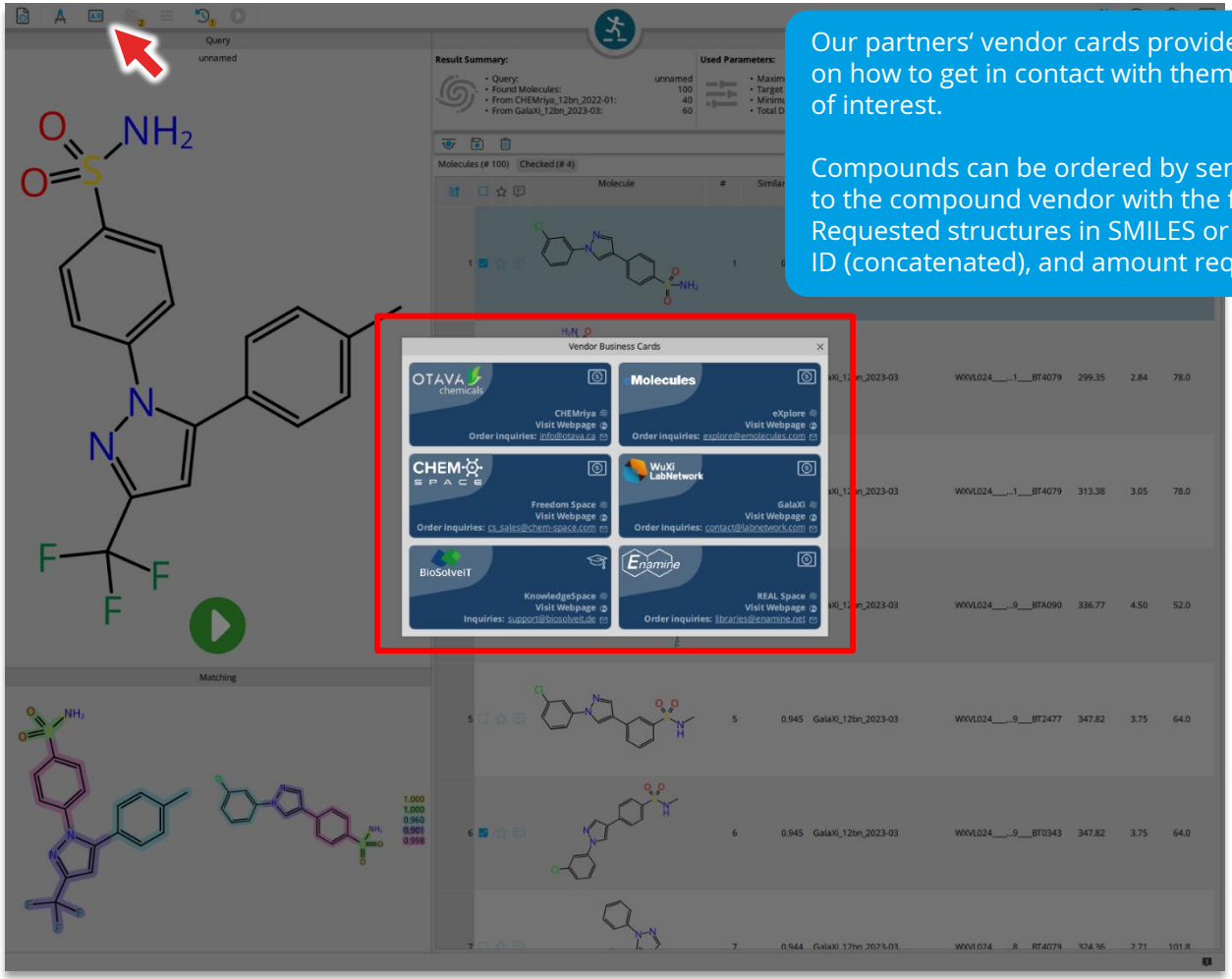


To protect your IP, any information about your query can be masked.

By default it is not masked, and information of your query will be included upon saving.

To mask your query, switch it to the green square.

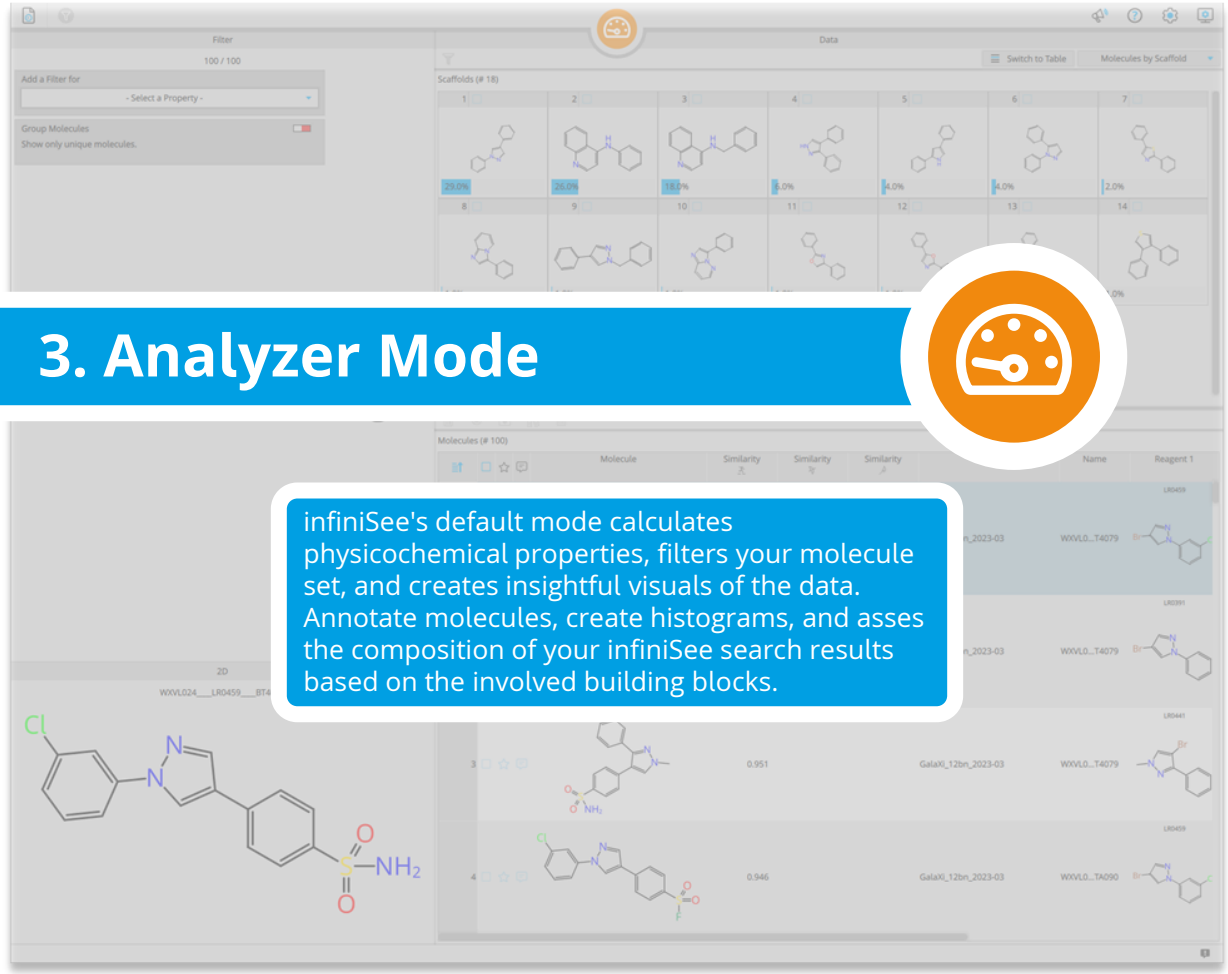
1. Click on the ‘Settings’ button.
2. Choose your desired export settings.
3. Press ‘Apply’.



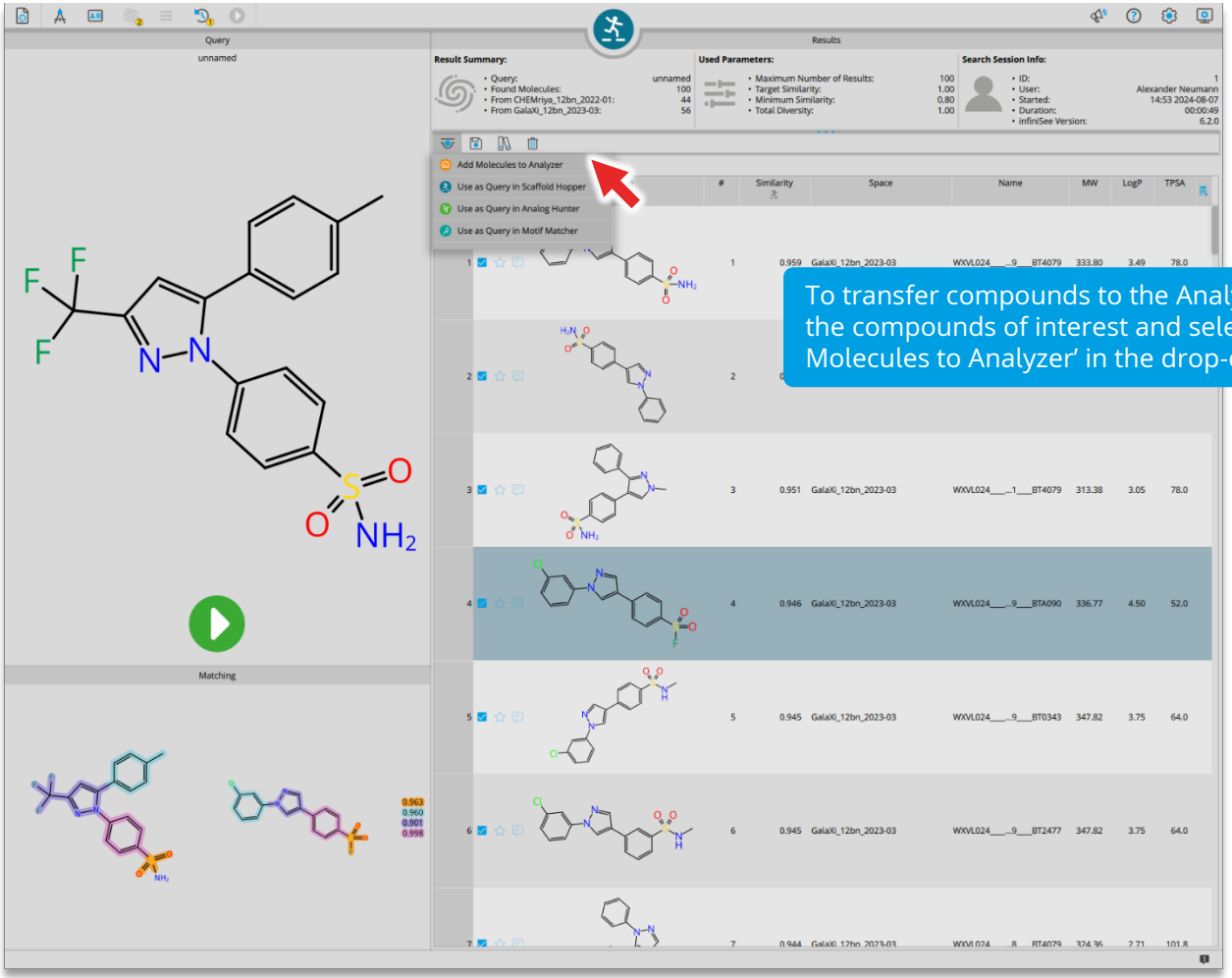
Our partners' vendor cards provide you with information on how to get in contact with them to order compounds of interest.

Compounds can be ordered by sending a quote request to the compound vendor with the following information: Requested structures in SMILES or SD format, Compound ID (concatenated), and amount requested.

3. Analyzer Mode

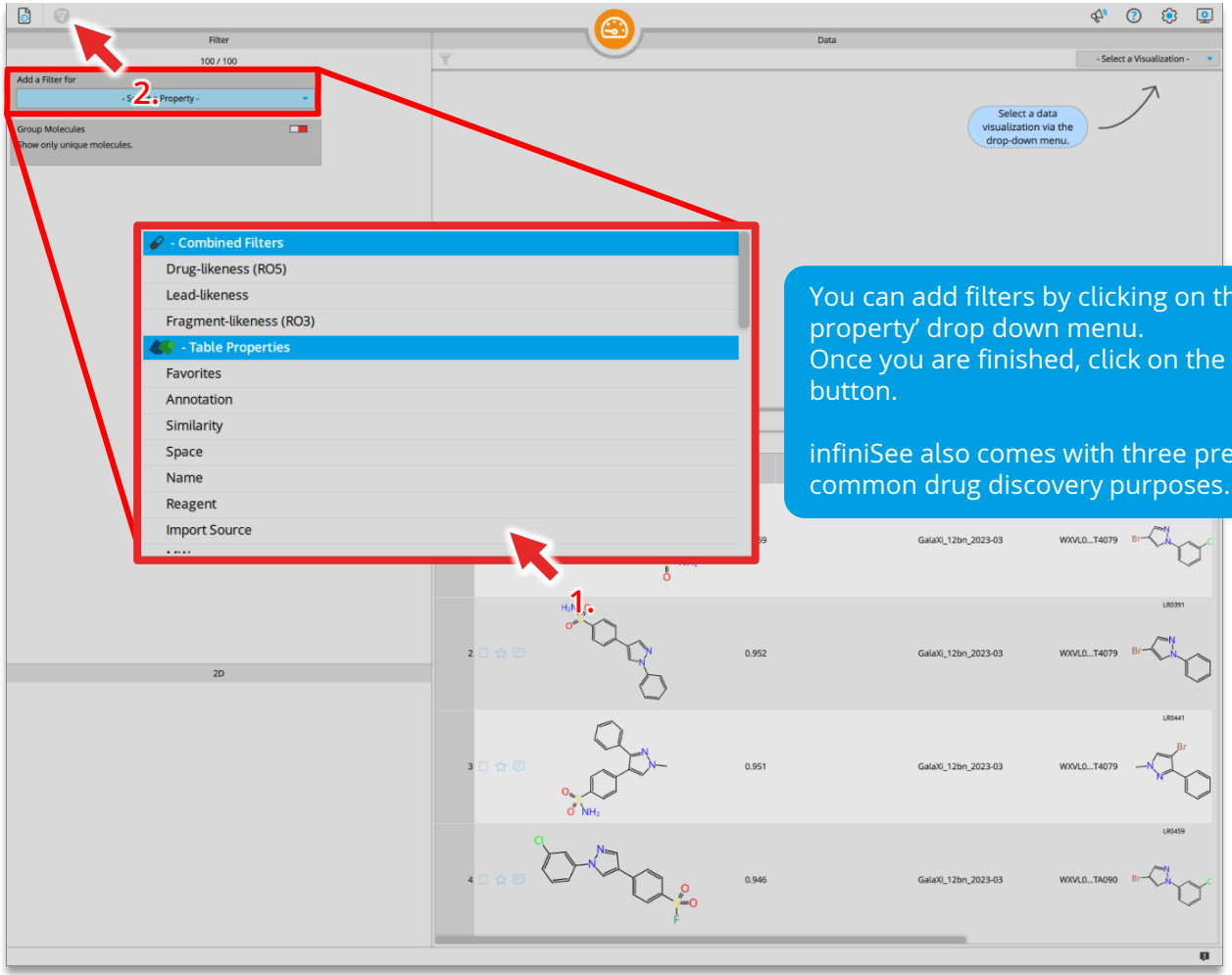


infiniSee's default mode calculates physicochemical properties, filters your molecule set, and creates insightful visuals of the data. Annotate molecules, create histograms, and asses the composition of your infiniSee search results based on the involved building blocks.



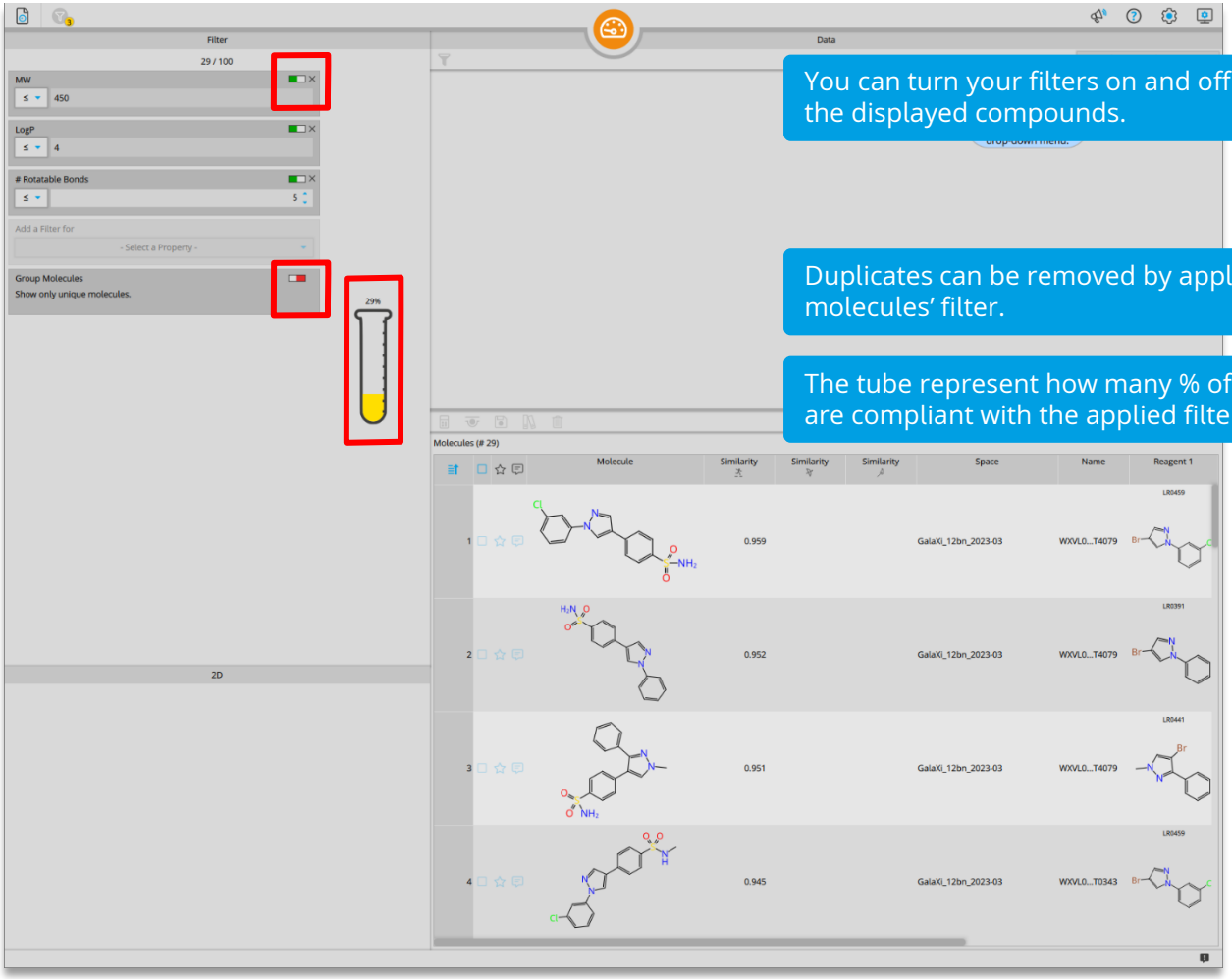
To transfer compounds to the Analyzer Mode, check the compounds of interest and select 'Add Molecules to Analyzer' in the drop-down menu.

... or hover over the mode button and select 'Analyzer'. Once in the Analyzer Mode you can load molecules (.sdf, .sd, .mol, .mol2, .smi, .smiles, .pdb formats) from a local folder directly into infiniSee.



You can add filters by clicking on the 'Select a property' drop down menu.
Once you are finished, click on the 'Apply filters' button.

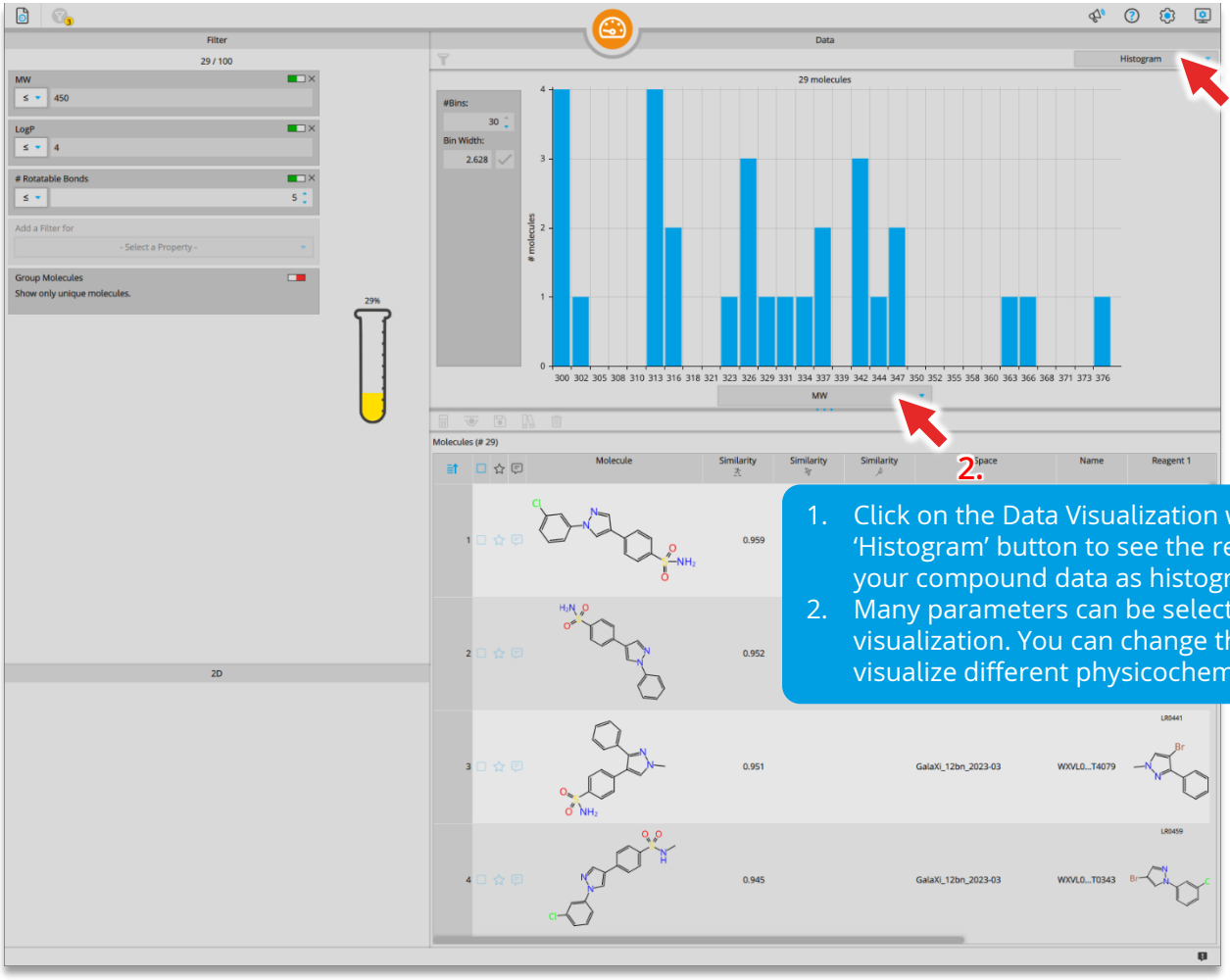
infiniSee also comes with three premade filters for common drug discovery purposes.



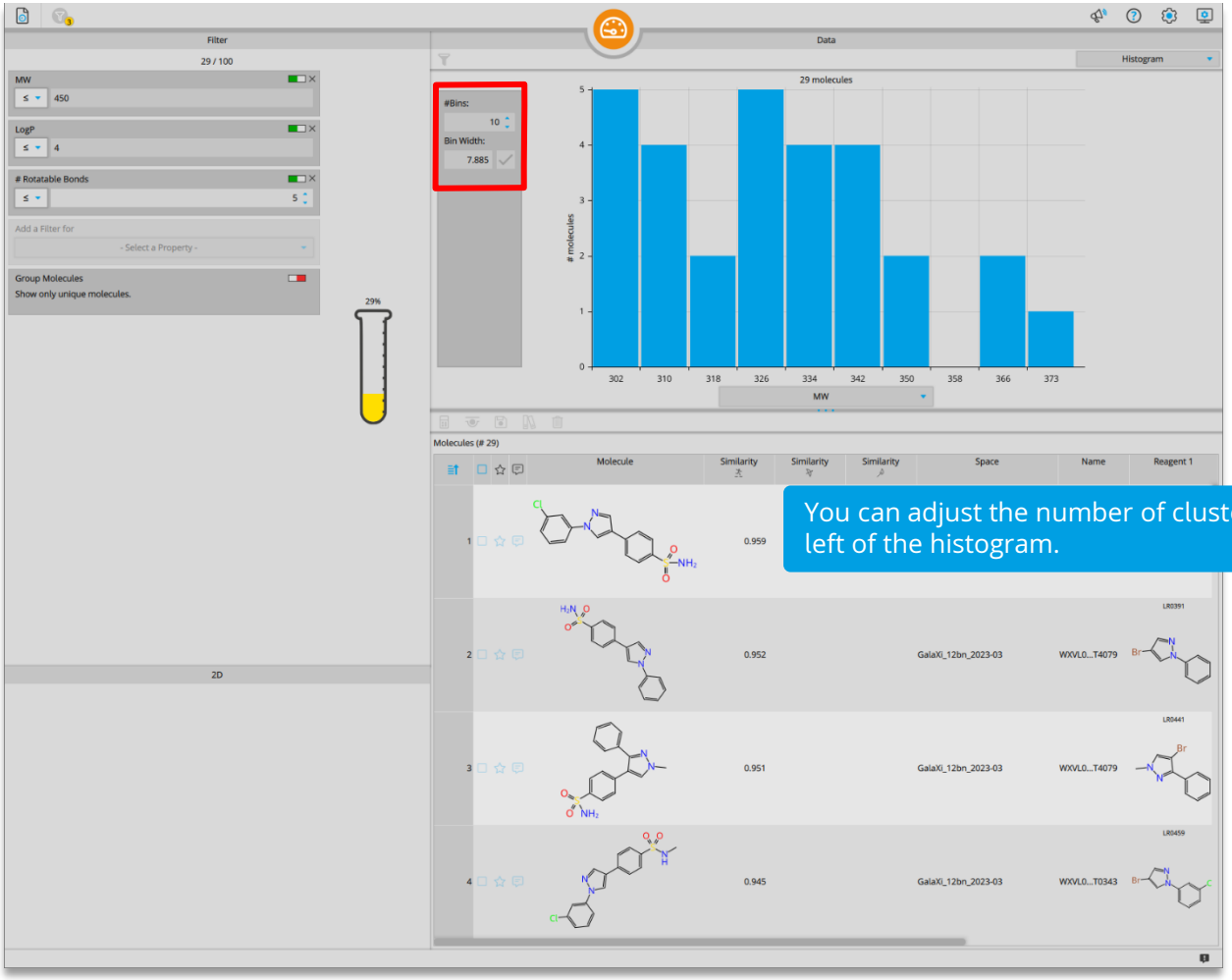
You can turn your filters on and off to manipulate the displayed compounds.

Duplicates can be removed by applying the 'Group molecules' filter.

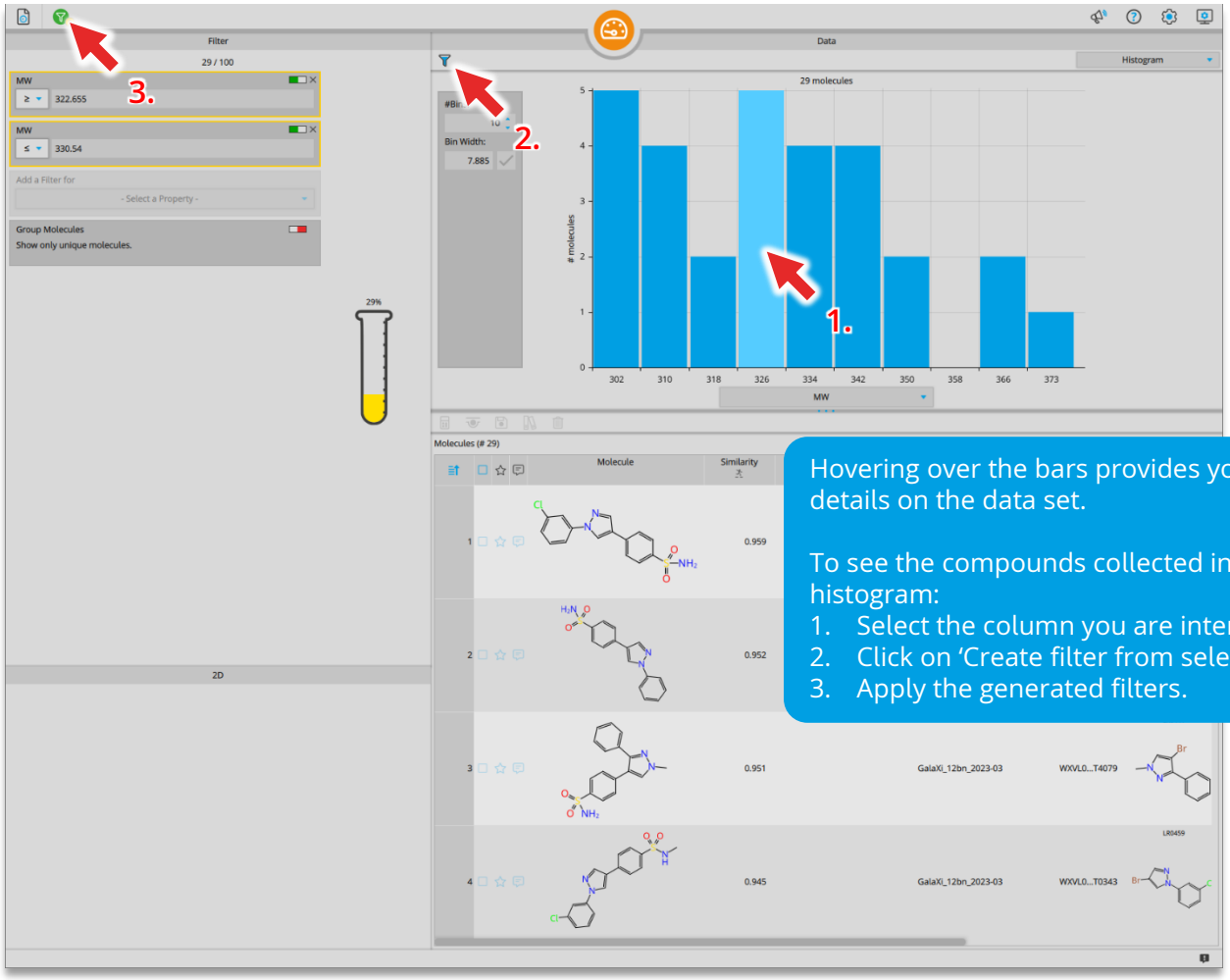
The tube represent how many % of the compounds are compliant with the applied filters.



1. Click on the Data Visualization window 'Histogram' button to see the representation of your compound data as histogram.
2. Many parameters can be selected for visualization. You can change the display to visualize different physicochemical properties.



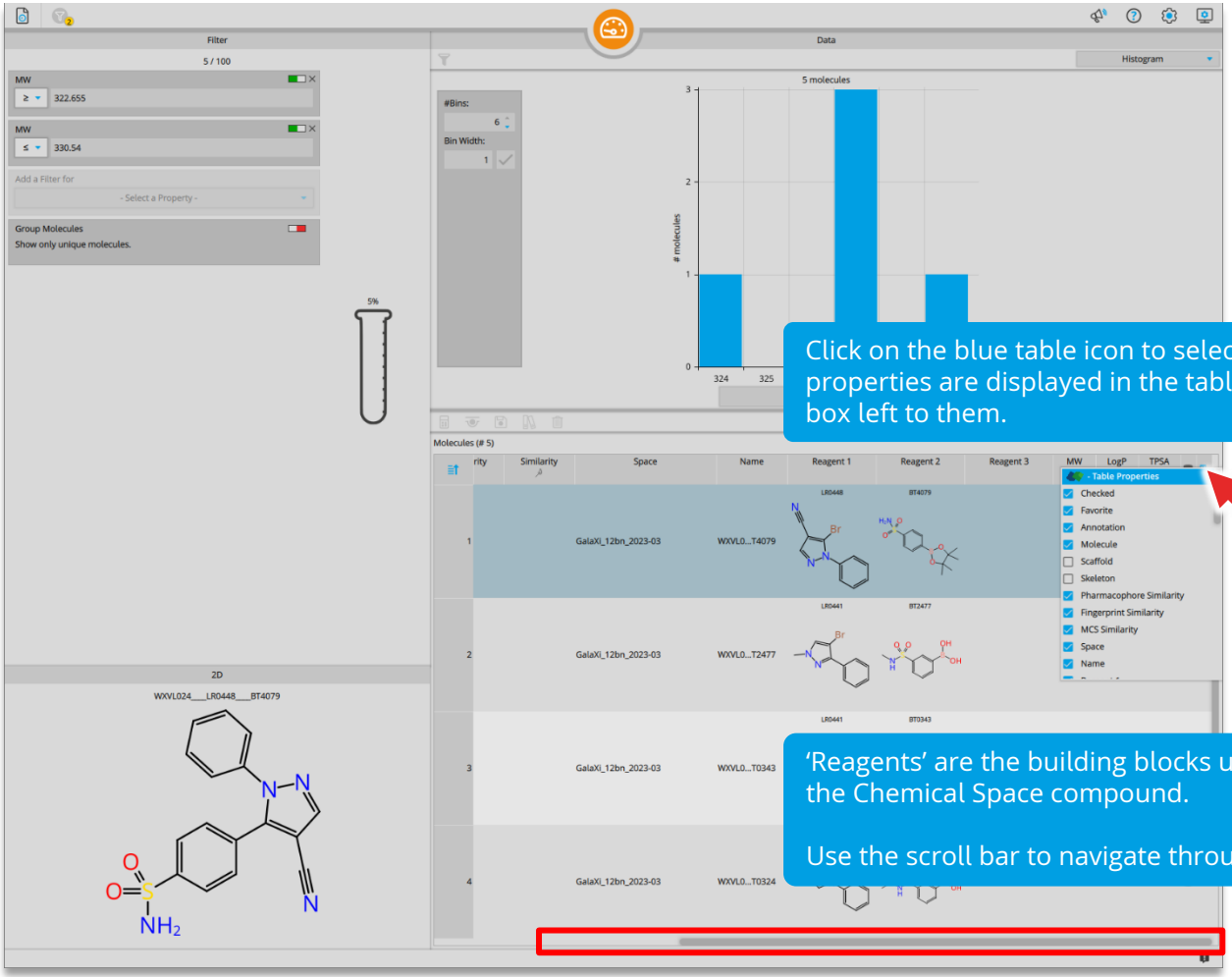
You can adjust the number of clustered bins to the left of the histogram.

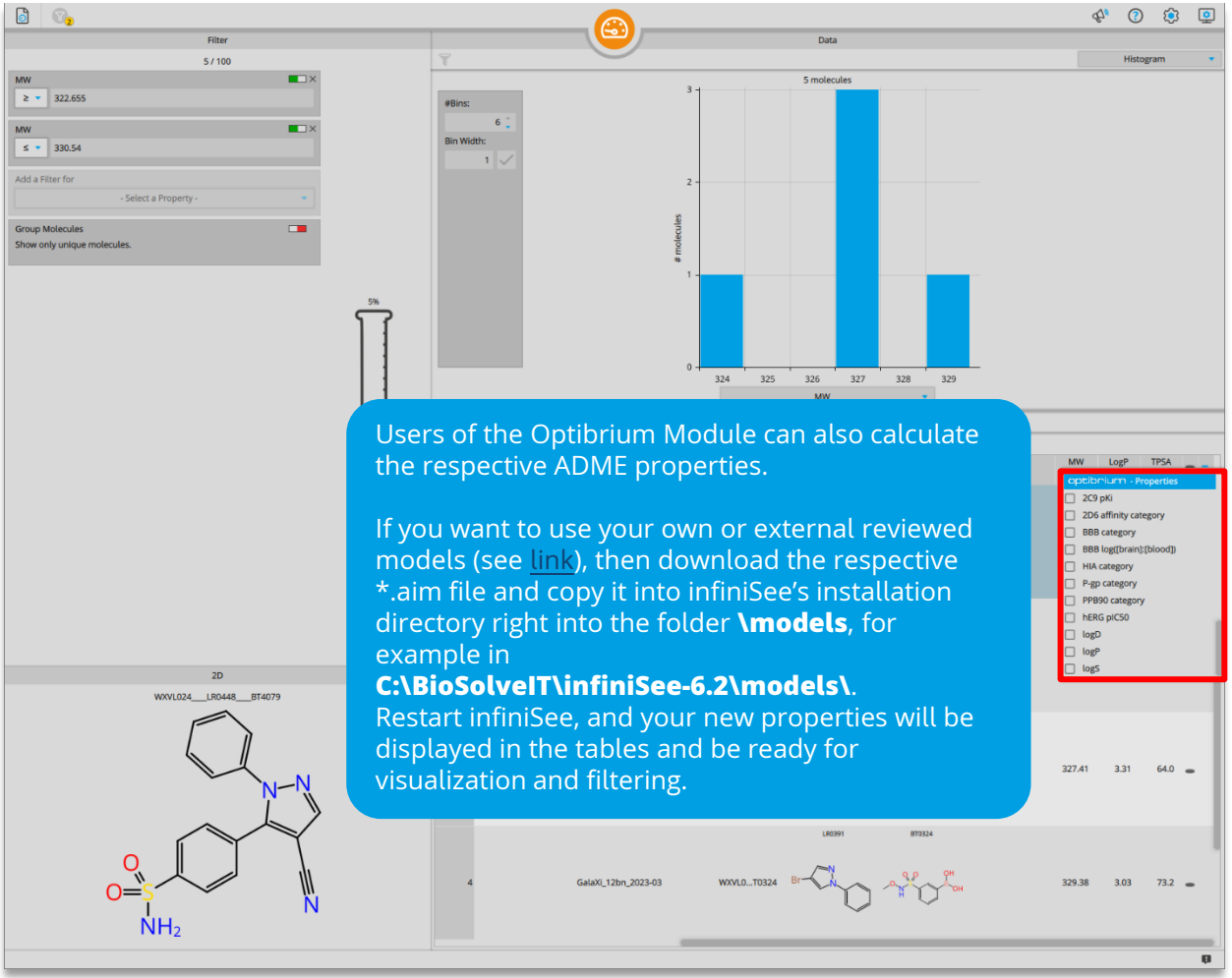


Hovering over the bars provides you with further details on the data set.

To see the compounds collected in a bar of the histogram:

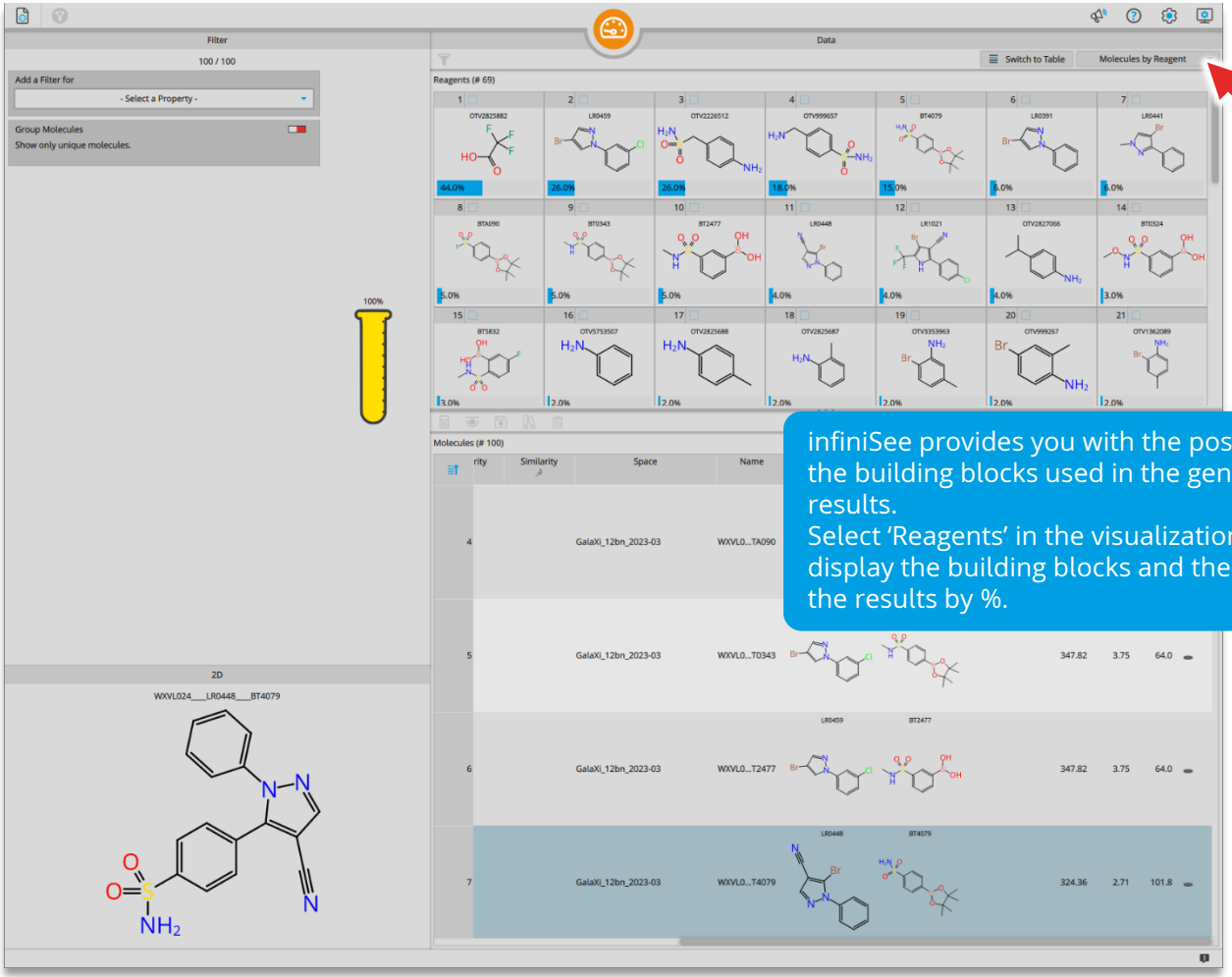
1. Select the column you are interested in.
2. Click on ‘Create filter from selection’.
3. Apply the generated filters.

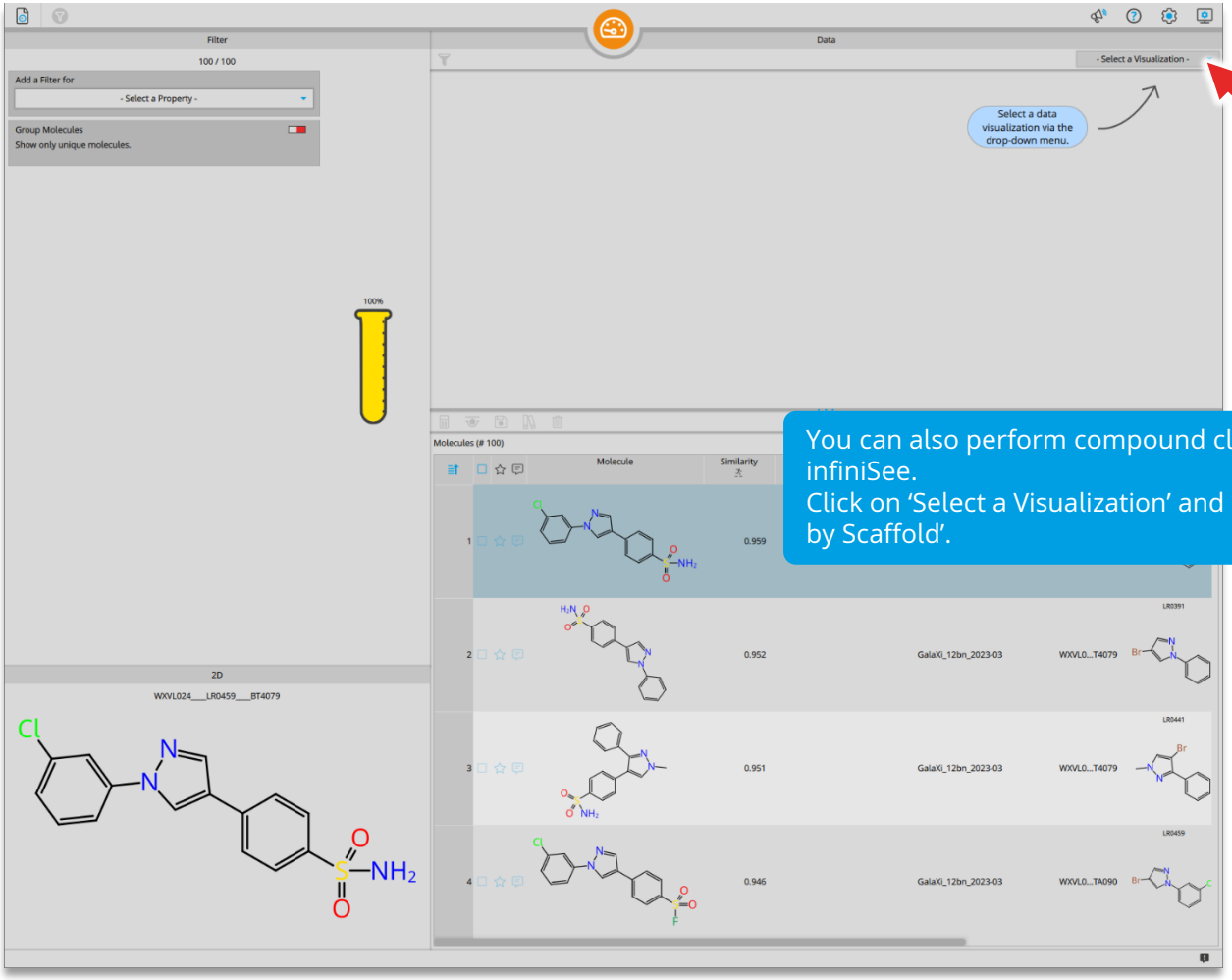

Filter
5 / 100
MW
≥ 322.655
MW
≤ 330.54
Add a Filter for
- Select a Property -
Group Molecules
Show only unique molecules.
5%
Data
Histogram
5 molecules
#Bins:
6
Bin Width:
1
molecules
Molecules (# 5)
Similarity
Space
Name
Reagent 1
Reagent 2
Reagent 3
MW
LogP
TPSA
- Table Properties
Checked
Favorite
Annotation
Molecule
Scaffold
Skeleton
Pharmacophore Similarity
Fingerprint Similarity
MCS Similarity
Space
Name
GalaXi_12bn_2023-03
2D
WXVL024___LR0448___BT4079
Click on the blue table icon to select which properties are displayed in the table by checking the box left to them.
'Reagents' are the building blocks used to synthesize the Chemical Space compound.
Use the scroll bar to navigate through your results.



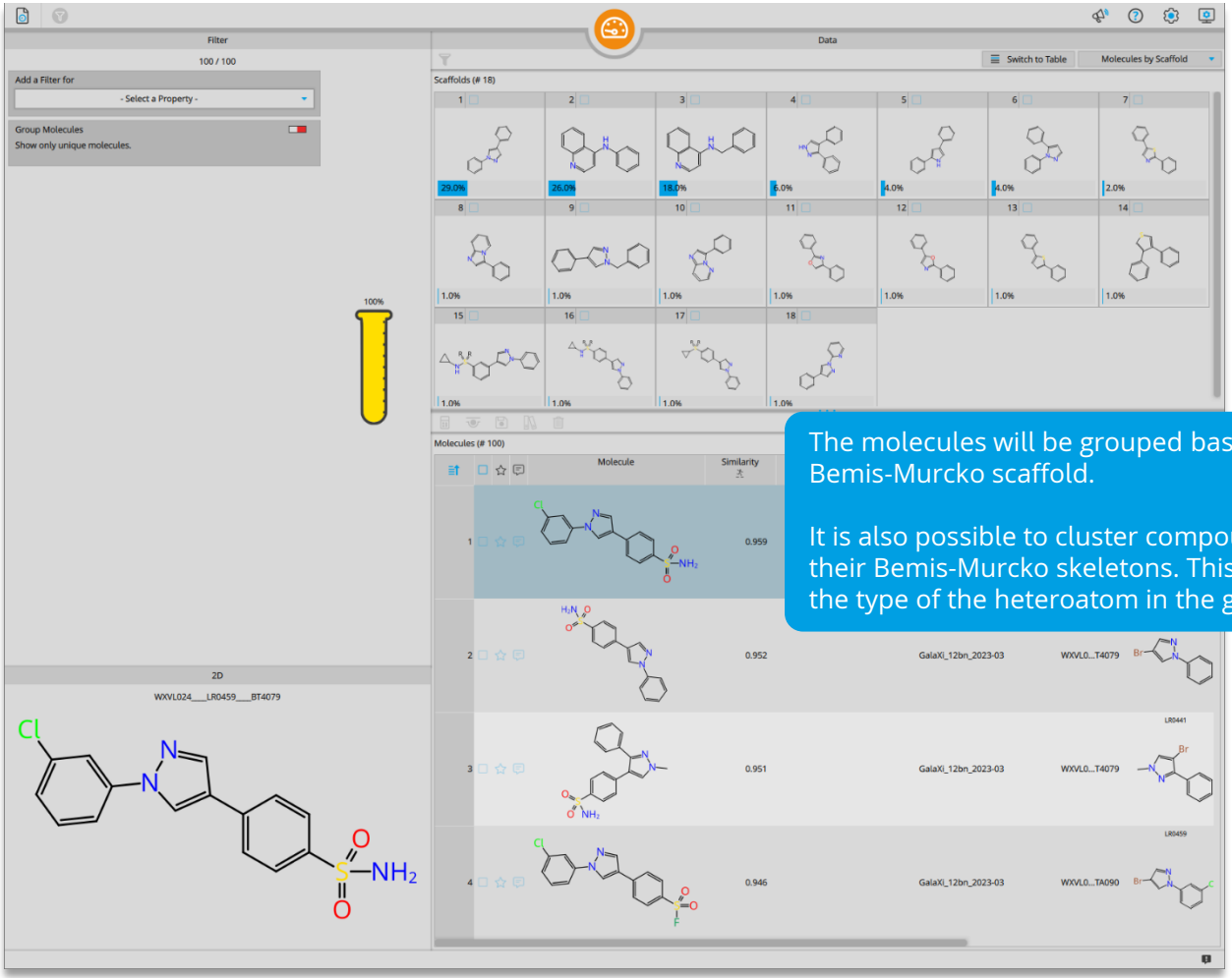
Users of the Optibrium Module can also calculate the respective ADME properties.

If you want to use your own or external reviewed models (see link), then download the respective *.aim file and copy it into infiniSee's installation directory right into the folder **\models**, for example in **C:\BioSolveIT\infiniSee-6.2\models**. Restart infiniSee, and your new properties will be displayed in the tables and be ready for visualization and filtering.


Filter
100 / 100
Add a Filter for
- Select a Property -
Group Molecules
Show only unique molecules.
Data
Switch to Table
Molecules by Reagent
Reagents (# 69)
100%
Molecules (# 100)
Space
Name
Similarity
GalaXi_12bn_2023-03
2D
WXVL024___LR0448___BT4079
infiniSee provides you with the possibility to assess the building blocks used in the generation of your results.
Select 'Reagents' in the visualization window to display the building blocks and their occurrence in the results by %.

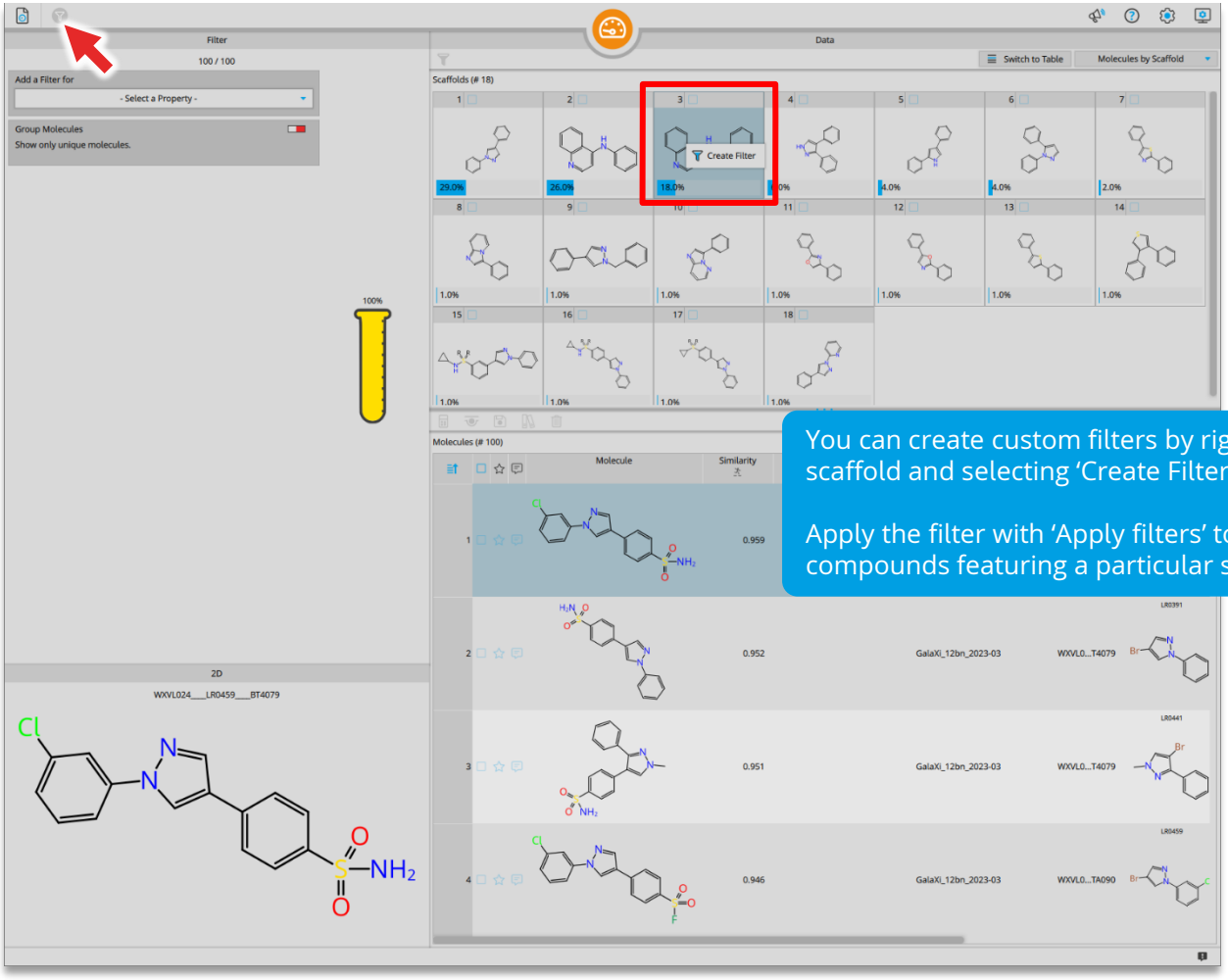


You can also perform compound clustering in infiniSee.
Click on 'Select a Visualization' and select 'Molecules by Scaffold'.



The molecules will be grouped based on their Bemis-Murcko scaffold.

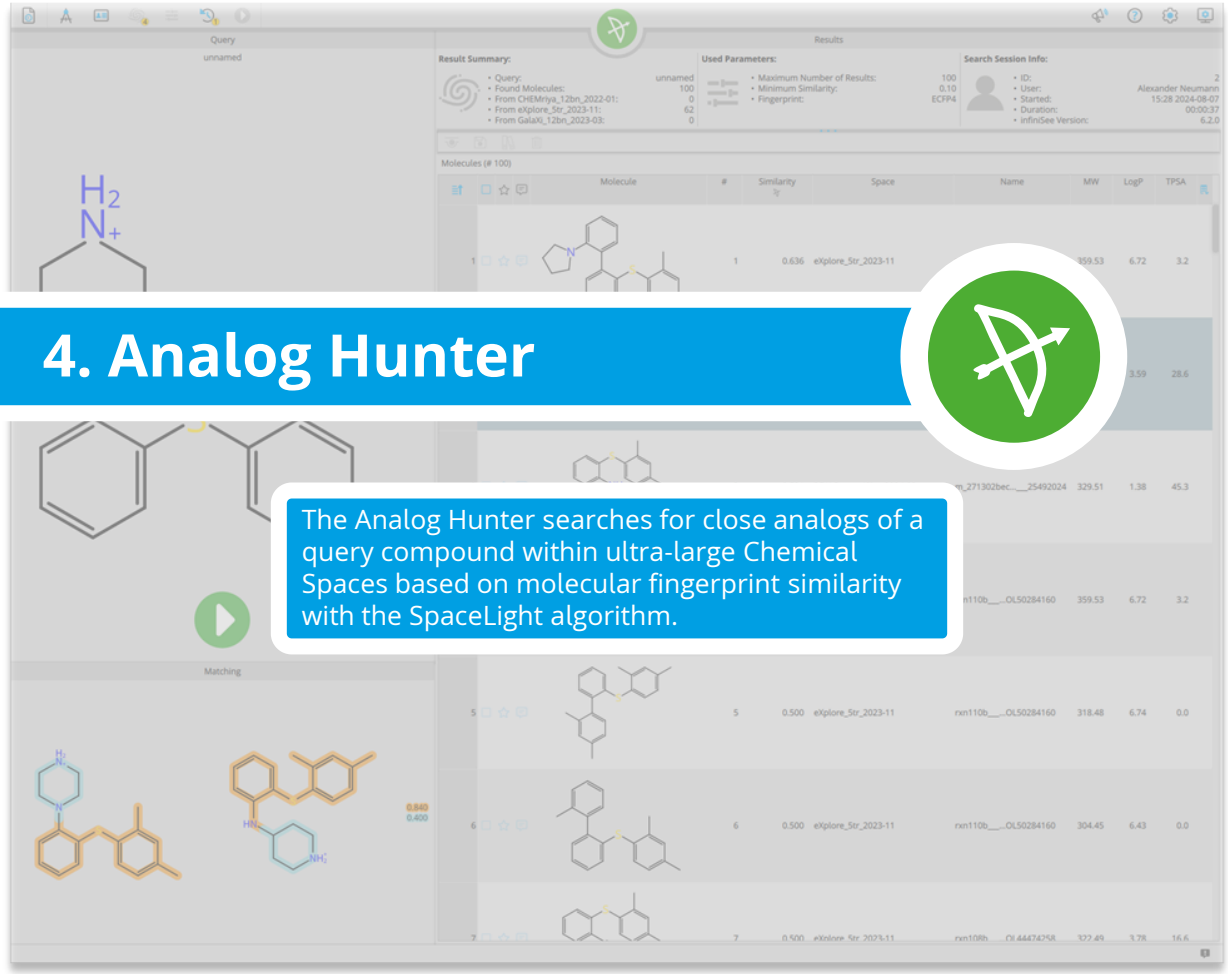
It is also possible to cluster compounds based on their Bemis-Murcko skeletons. This method ignores the type of the heteroatom in the grouping process.



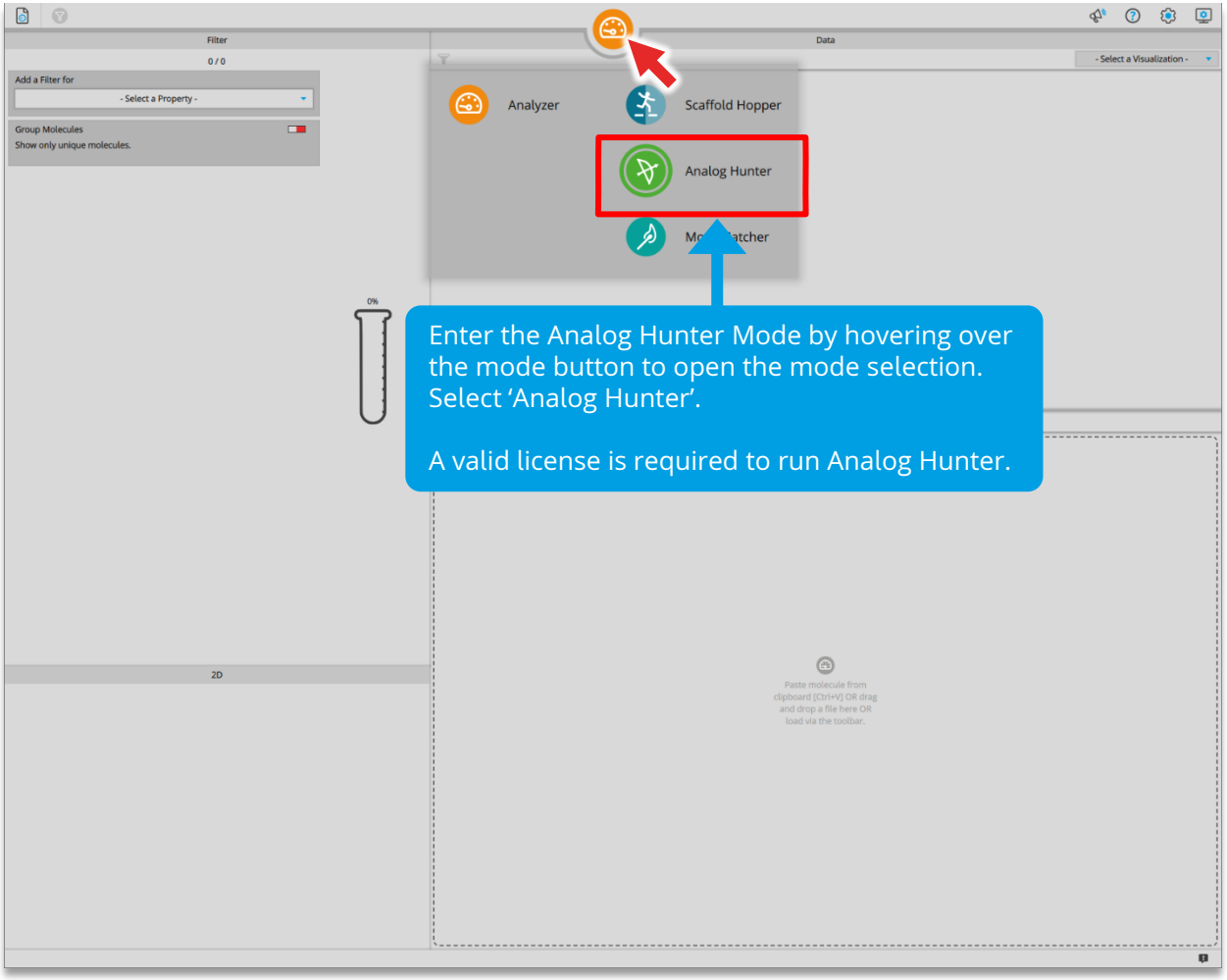
You can create custom filters by right-clicking on a scaffold and selecting ‘Create Filter’.

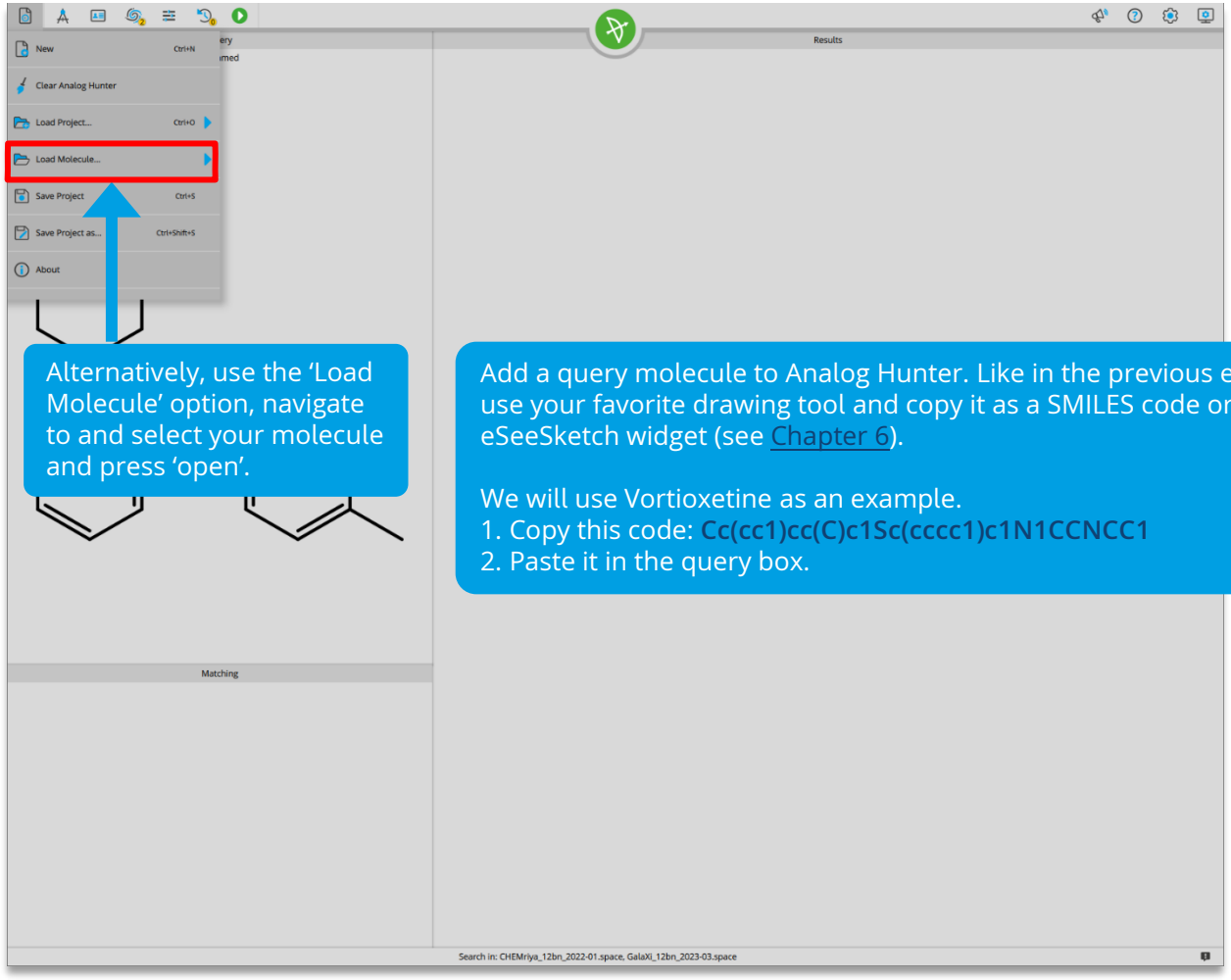
Apply the filter with ‘Apply filters’ to see only the compounds featuring a particular scaffold.

4. Analog Hunter



The Analog Hunter searches for close analogs of a query compound within ultra-large Chemical Spaces based on molecular fingerprint similarity with the SpaceLight algorithm.

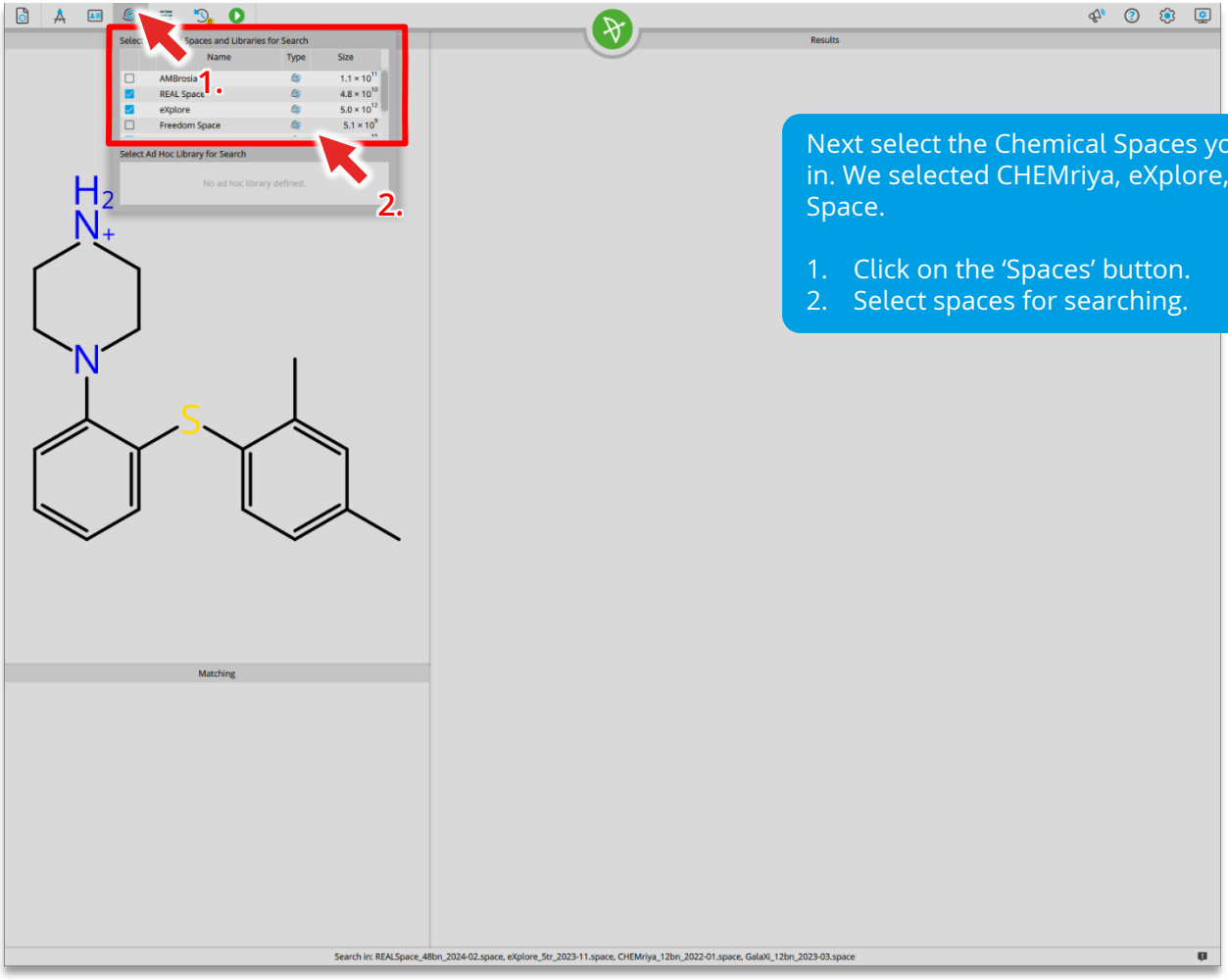

Filter
0 / 0
Add a Filter for
- Select a Property -
Group Molecules
Show only unique molecules.
Data
- Select a Visualization -
Analyzer
Scaffold Hopper
Analog Hunter
0%
2D
Paste molecule from clipboard (Ctrl+V) OR drag and drop a file here OR load via the toolbar.
Enter the Analog Hunter Mode by hovering over the mode button to open the mode selection. Select 'Analog Hunter'.
A valid license is required to run Analog Hunter.



Alternatively, use the 'Load Molecule' option, navigate to and select your molecule and press 'open'.

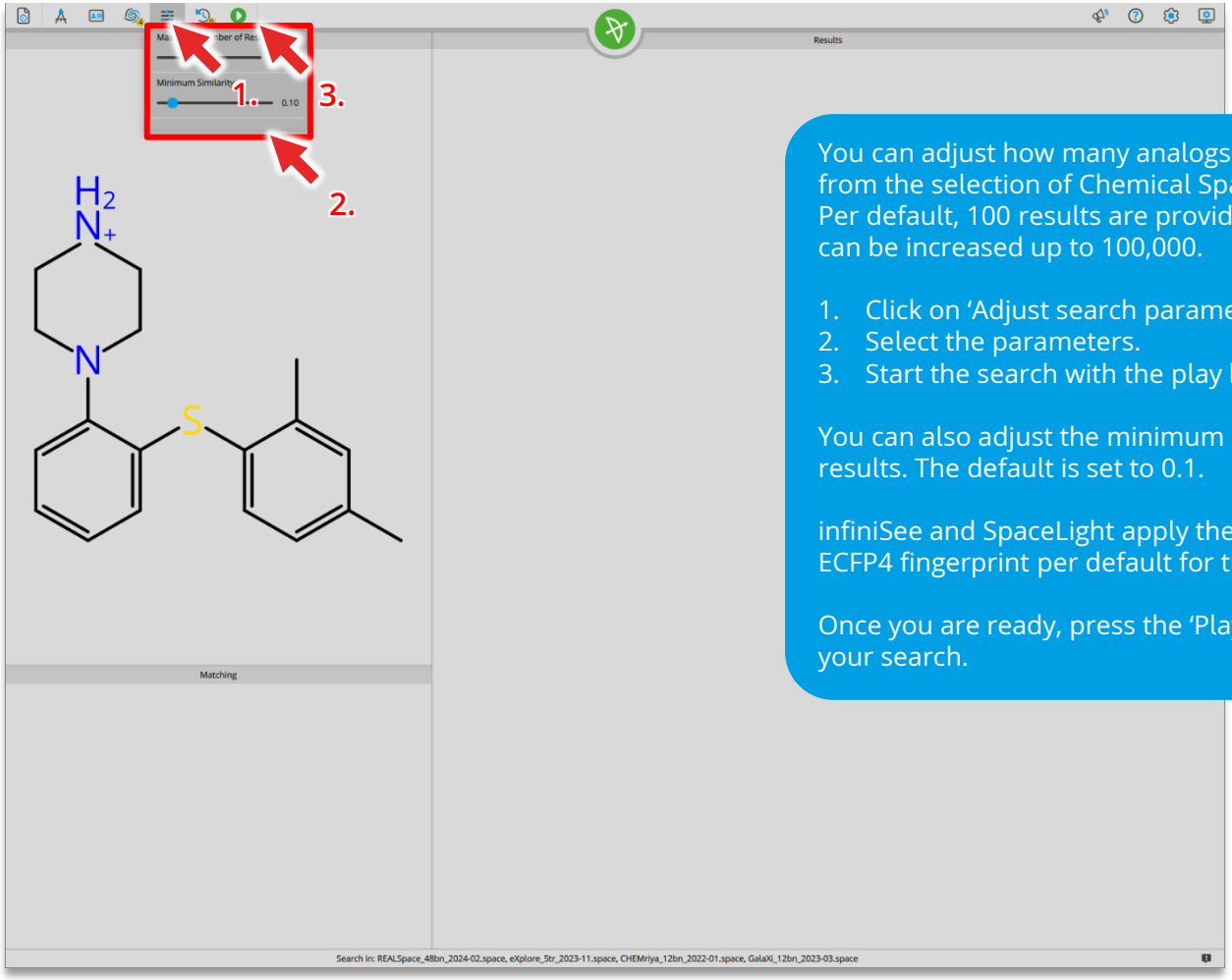
Add a query molecule to Analog Hunter. Like in the previous example, you may use your favorite drawing tool and copy it as a SMILES code or use the eSeeSketch widget (see Chapter 6).

We will use Vortioxetine as an example.
1. Copy this code: **Cc(cc1)cc(C)c1Sc(cccc1)c1N1CCNCC1**
2. Paste it in the query box.



Next select the Chemical Spaces you want to search in. We selected CHEMriya, eXplore, GalaXi and REAL Space.

1. Click on the 'Spaces' button.
2. Select spaces for searching.



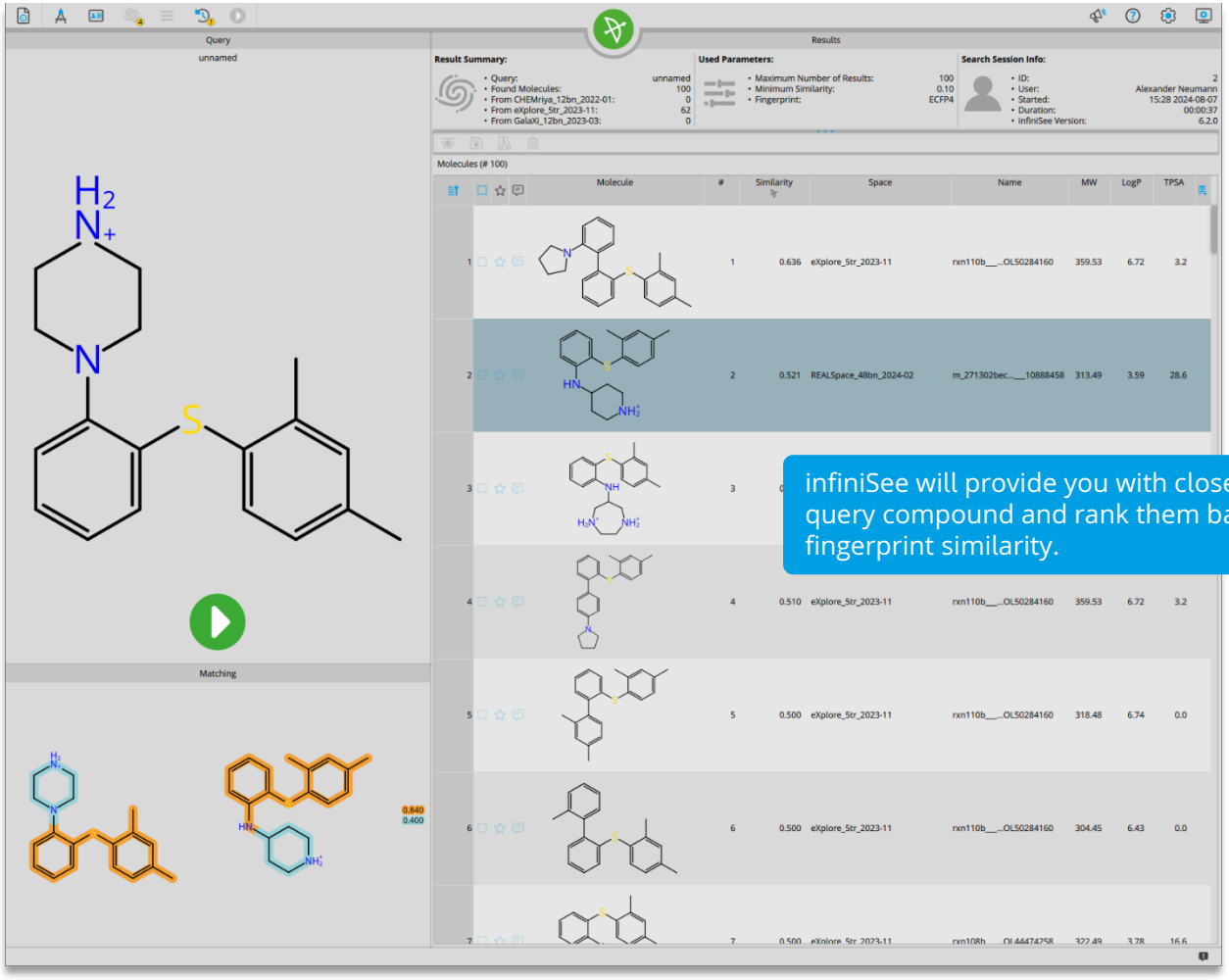
You can adjust how many analogs are retrieved from the selection of Chemical Spaces.
Per default, 100 results are provided. The number can be increased up to 100,000.

1. Click on ‘Adjust search parameters’
2. Select the parameters.
3. Start the search with the play button!

You can also adjust the minimum similarity of the results. The default is set to 0.1.

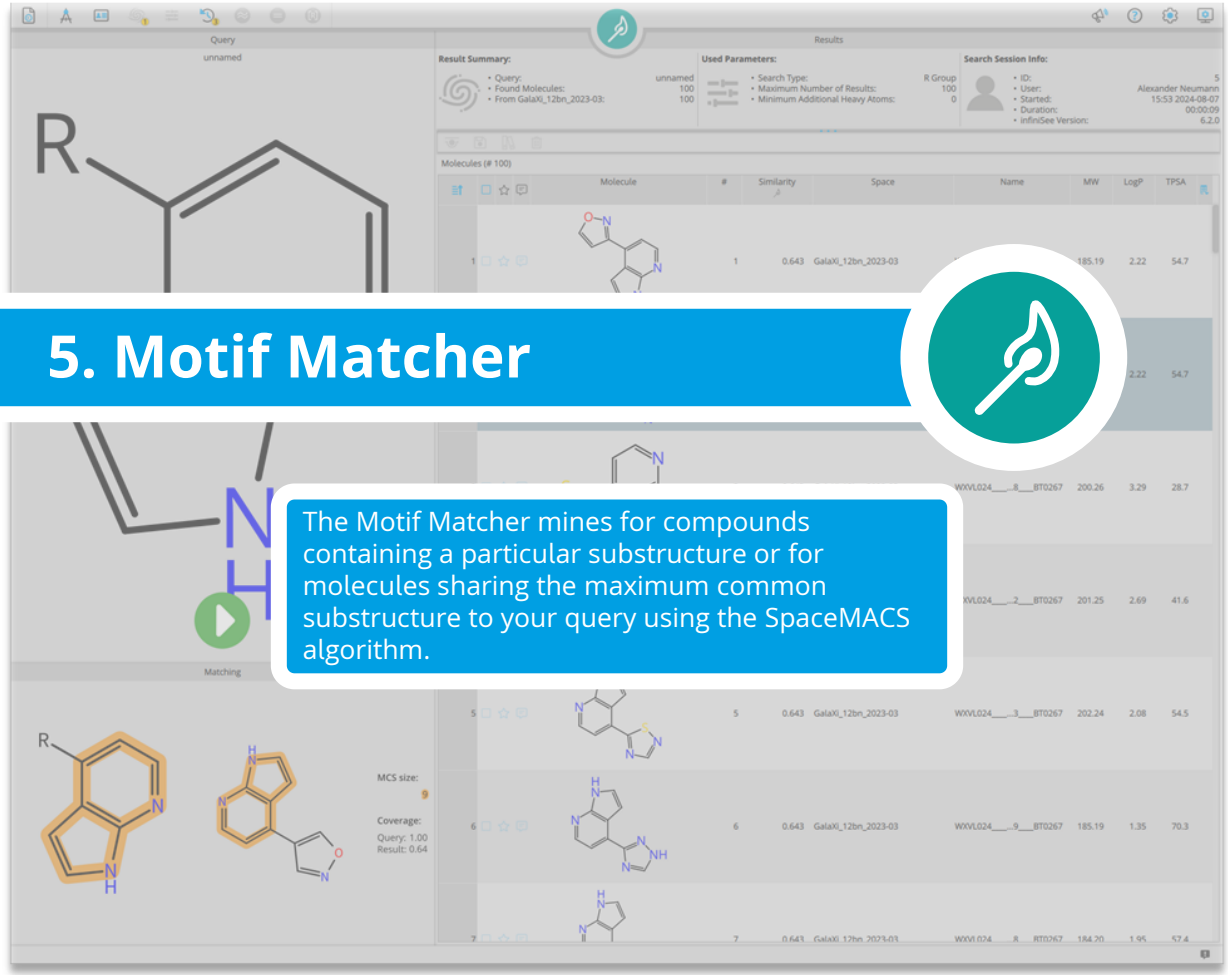
infiniSee and SpaceLight apply the well-known ECFP4 fingerprint per default for the search.

Once you are ready, press the ‘Play’ button to start your search.

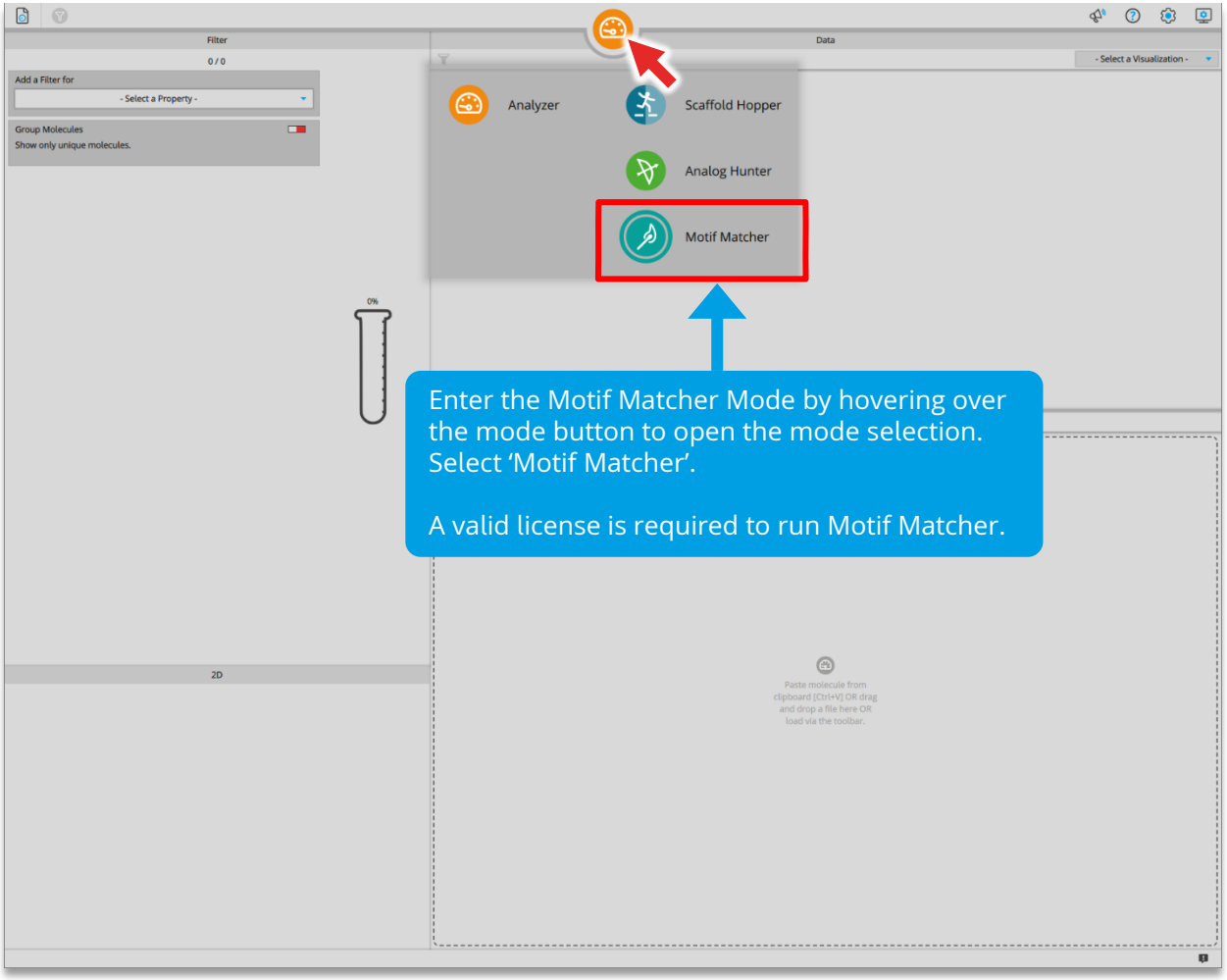


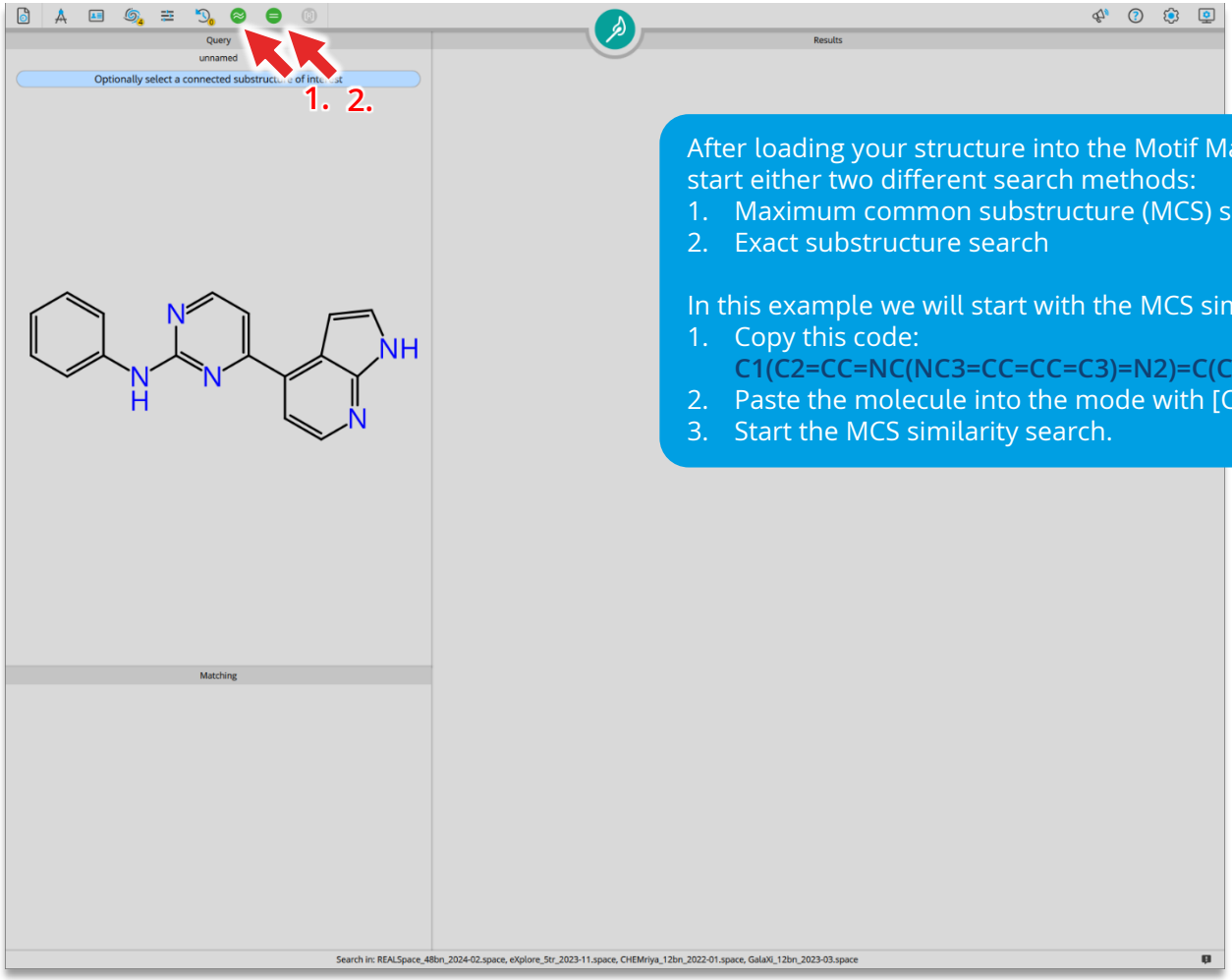
infiniSee will provide you with close analogs to your query compound and rank them based on their fingerprint similarity.

5. Motif Matcher



The Motif Matcher mines for compounds containing a particular substructure or for molecules sharing the maximum common substructure to your query using the SpaceMACS algorithm.


Filter
0 / 0
Add a Filter for
- Select a Property -
Group Molecules
Show only unique molecules.
Data
- Select a Visualization -
Analyzer
Scaffold Hopper
Analog Hunter
Motif Matcher
0%
2D
Paste molecule from clipboard (Ctrl+V) OR drag and drop a file here OR load via the toolbar.
Enter the Motif Matcher Mode by hovering over the mode button to open the mode selection. Select 'Motif Matcher'.
A valid license is required to run Motif Matcher.

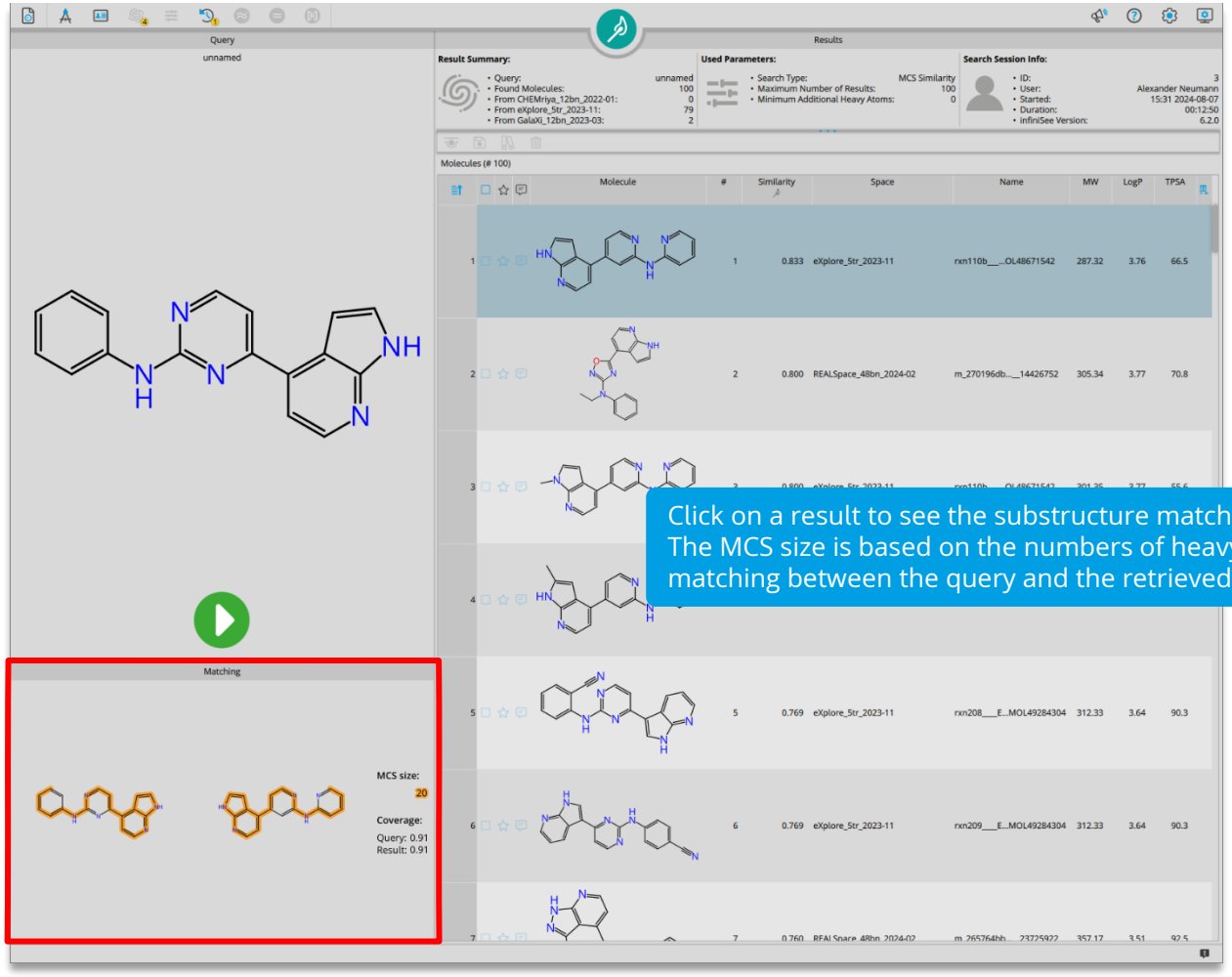


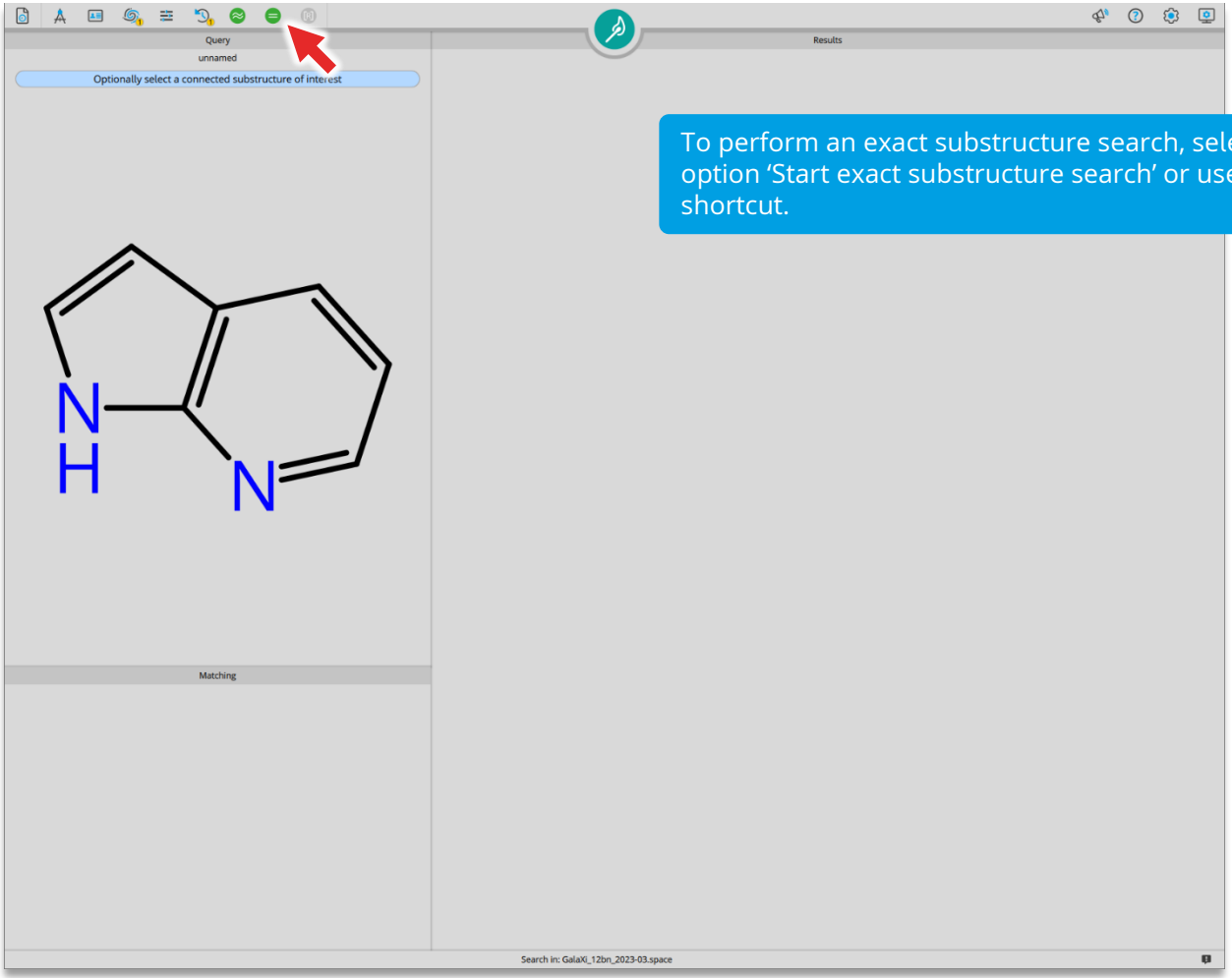
After loading your structure into the Motif Matcher, you can start either two different search methods:

1. Maximum common substructure (MCS) similarity search
2. Exact substructure search

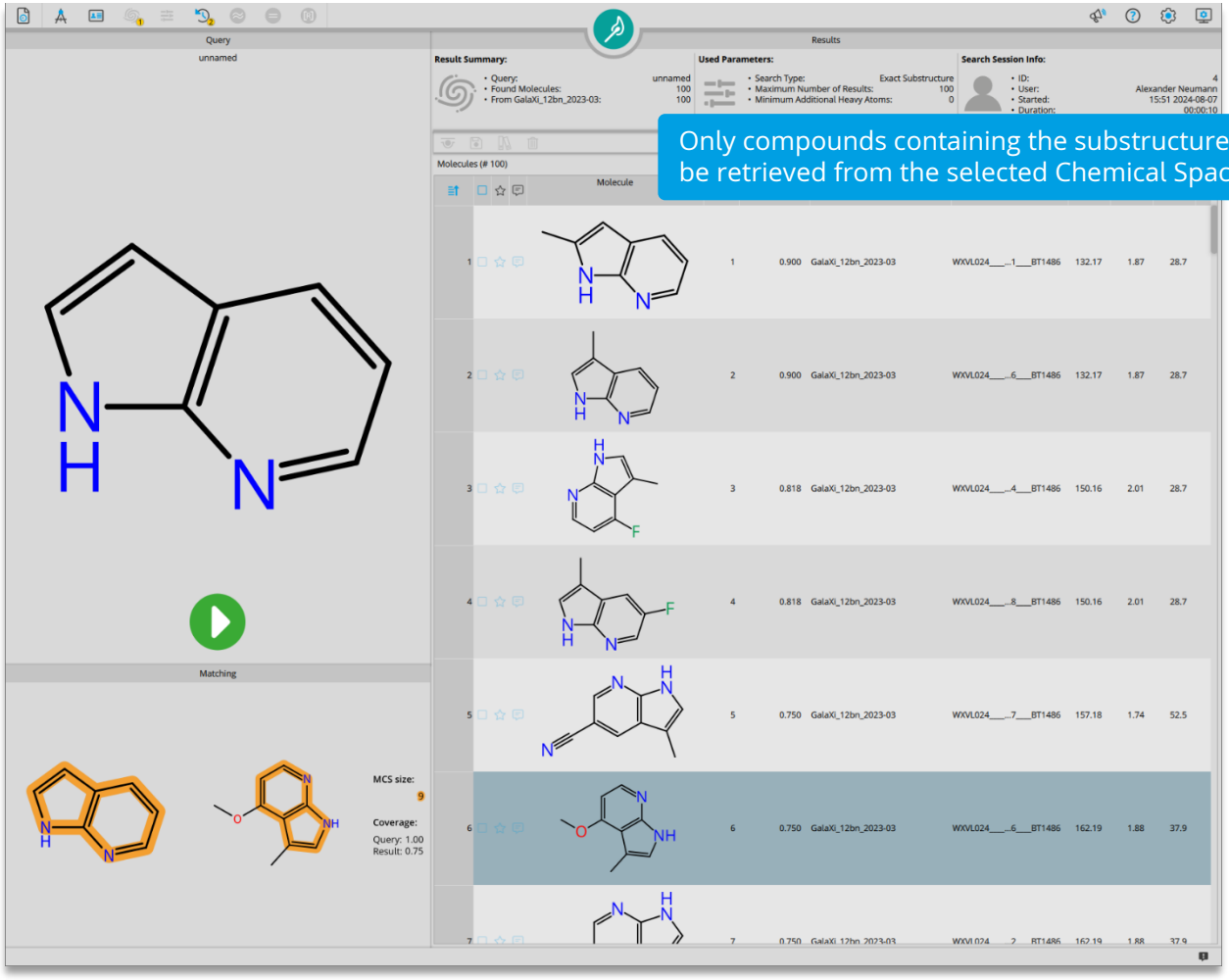
In this example we will start with the MCS similarity search.

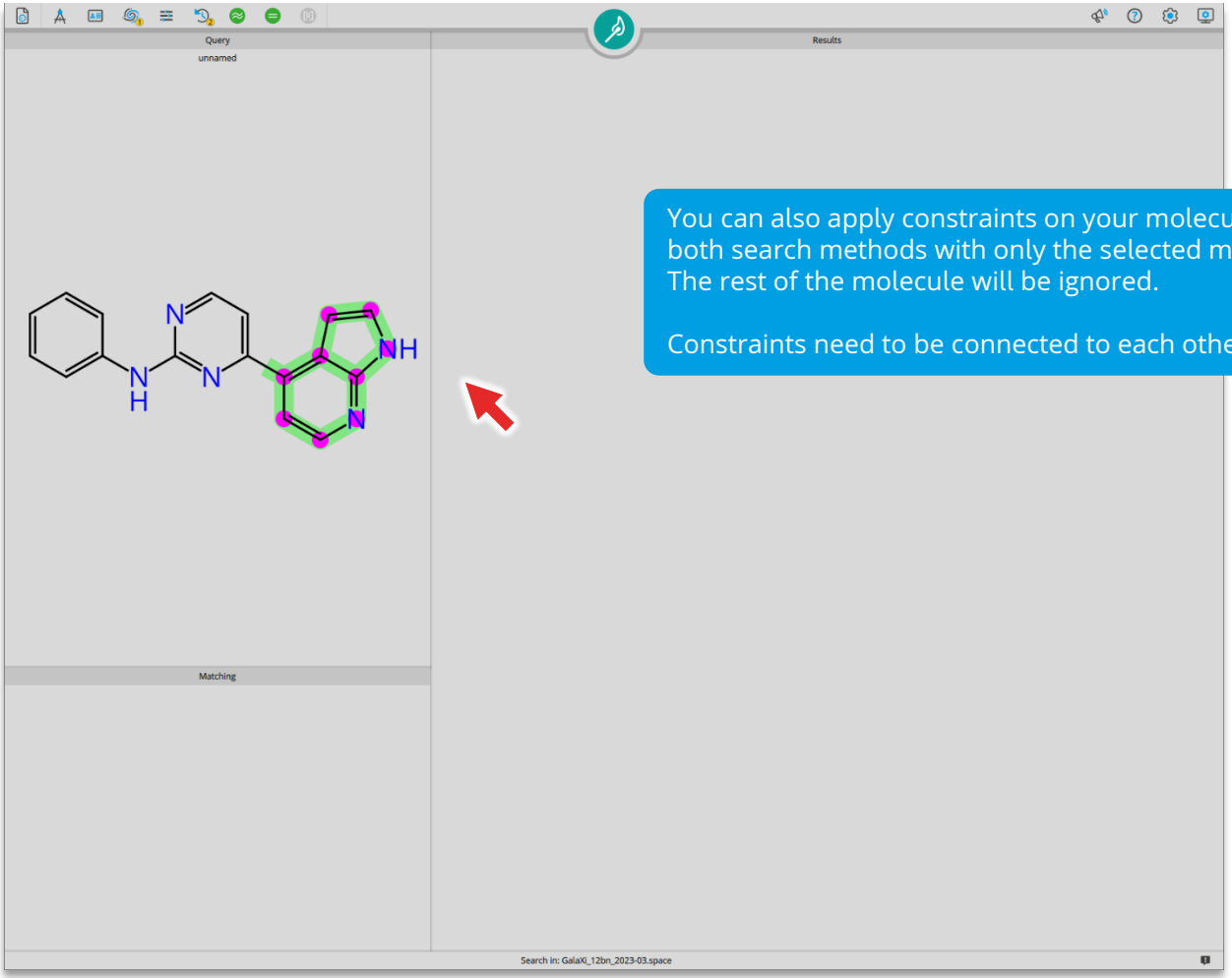
1. Copy this code:
   C1(C2=CC=NC(NC3=CC=CC=C3)=N2)=C(C=CN4)C4=NC=C1
2. Paste the molecule into the mode with [Ctrl+V]
3. Start the MCS similarity search.


Query
unnamed
Results
Result Summary:
• Query: unnamed
• Found Molecules: 100
• From CHEMriya_12bn_2022-01: 0
• From eXplore_5tr_2023-11: 79
• From GalaXi_12bn_2023-03: 2
Used Parameters:
• Search Type: MCS Similarity
• Maximum Number of Results: 100
• Minimum Additional Heavy Atoms: 0
Search Session Info:
• ID: 3
• User: Alexander Neumann
• Started: 15:31 2024-08-07
• Duration: 00:12:50
• infiniSee Version: 6.2.0
Molecules (# 100)
Molecule
#
Similarity
Space
Name
MW
LogP
TPSA
1 1 0.833 eXplore_5tr_2023-11 rxn110b___..OL48671542 287.32 3.76 66.5
2 2 0.800 REALSpace_48bn_2024-02 m_270196db..._14426752 305.34 3.77 70.8
3
4
5 5 0.769 eXplore_5tr_2023-11 rxn208___E...MOL49284304 312.33 3.64 90.3
6 6 0.769 eXplore_5tr_2023-11 rxn209___E...MOL49284304 312.33 3.64 90.3
7 7 0.760 REALSpace_48bn_2024-02 m_265764bb..._23725922 357.17 3.51 92.5
Matching
MCS size:
20
Coverage:
Query: 0.91
Result: 0.91
Click on a result to see the substructure matching.
The MCS size is based on the numbers of heavy atoms matching between the query and the retrieved compound.



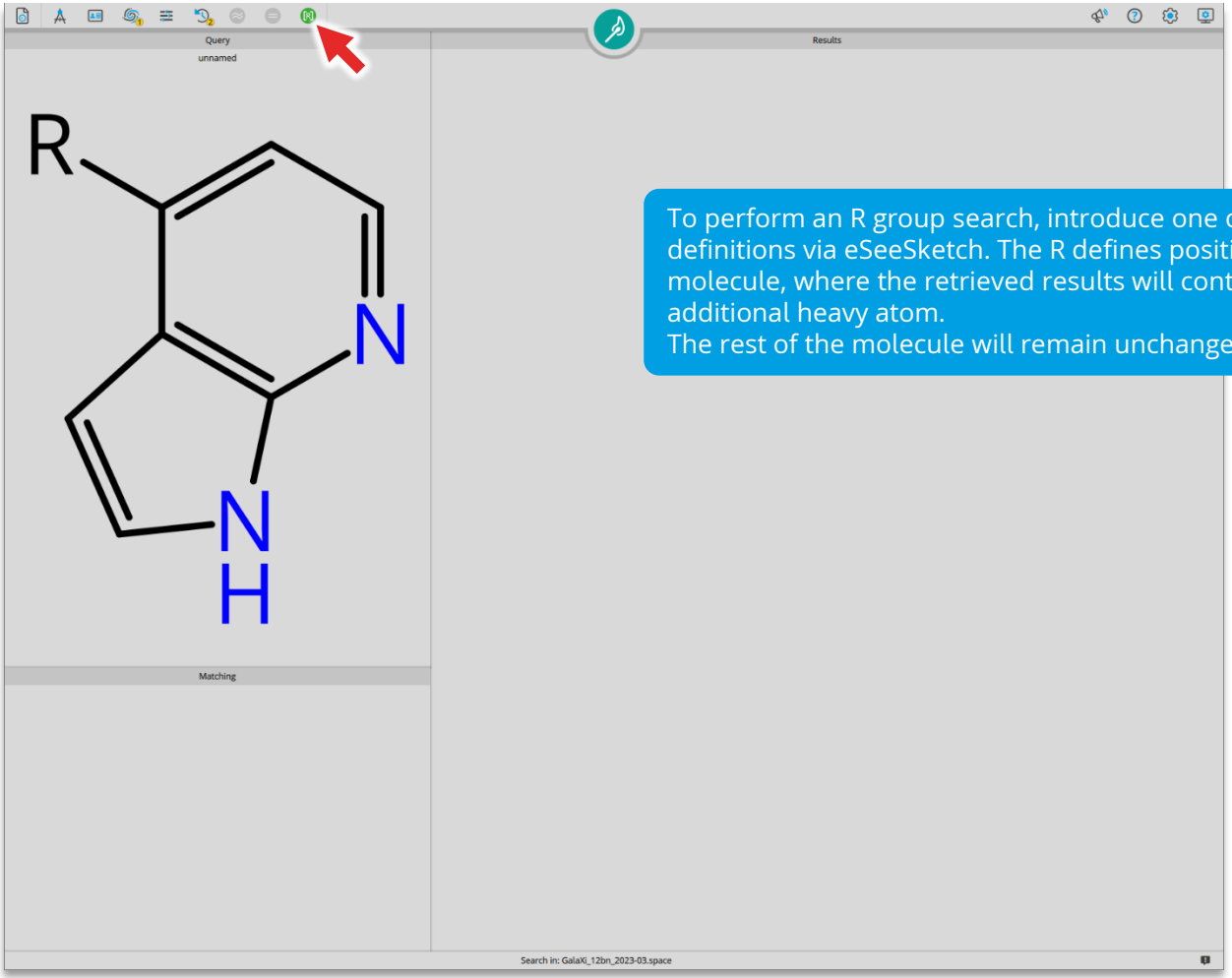
To perform an exact substructure search, select the second option ‘Start exact substructure search’ or use the [Ctrl+E] shortcut.


Query
unnamed
Results
Result Summary:
• Query: unnamed
• Found Molecules: 100
• From GalaXi_12bn_2023-03: 100
Used Parameters:
• Search Type: Exact Substructure
• Maximum Number of Results: 100
• Minimum Additional Heavy Atoms: 0
Search Session Info:
• ID: 4
• User: Alexander Neumann
• Started: 15:51 2024-08-07
• Duration: 00:00:10
Only compounds containing the substructure of interest will be retrieved from the selected Chemical Space.
Molecules (# 100)
Molecule
Matching
MCS size:
9
Coverage:
Query: 1.00
Result: 0.75

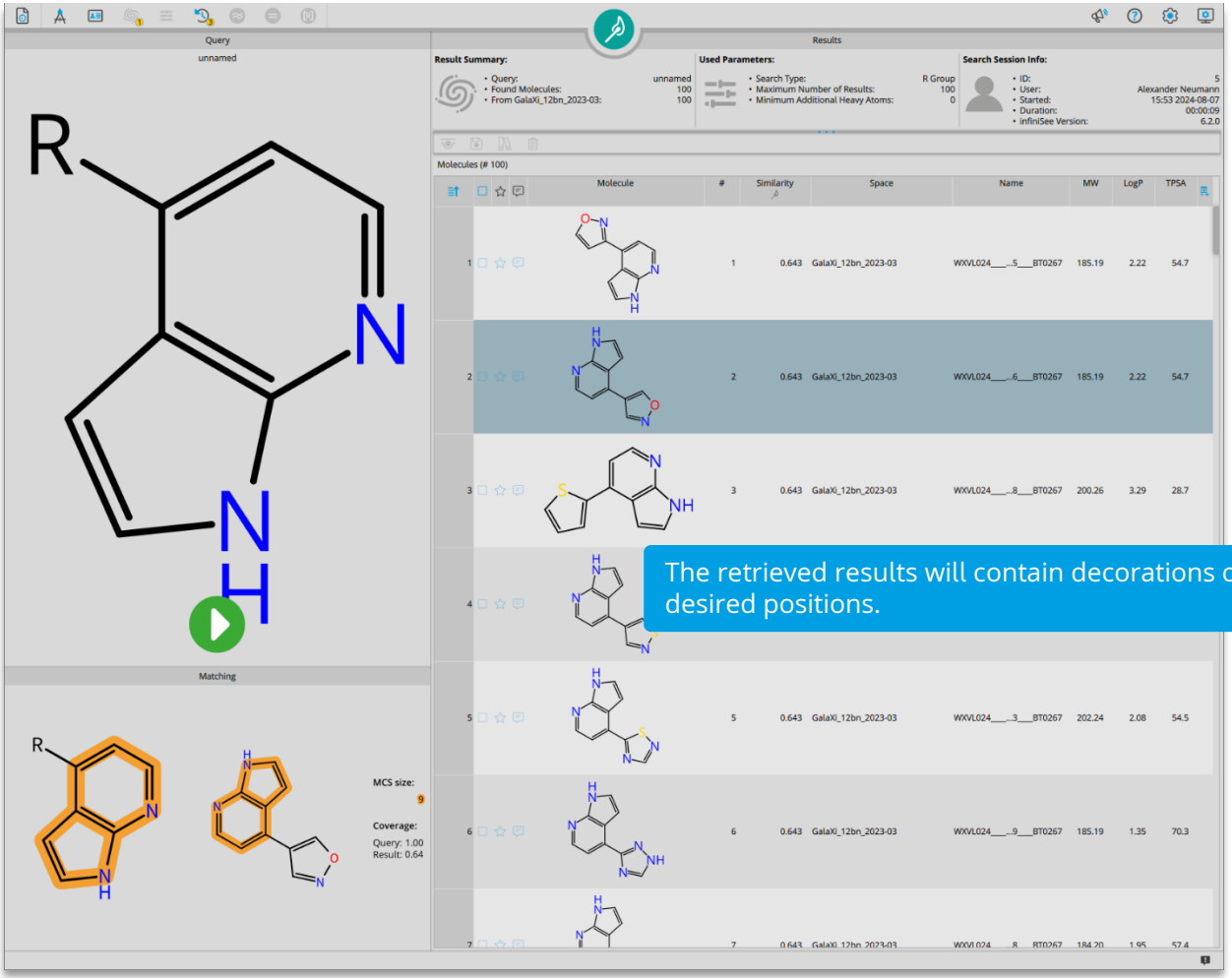


You can also apply constraints on your molecule to perform both search methods with only the selected moieties.
The rest of the molecule will be ignored.

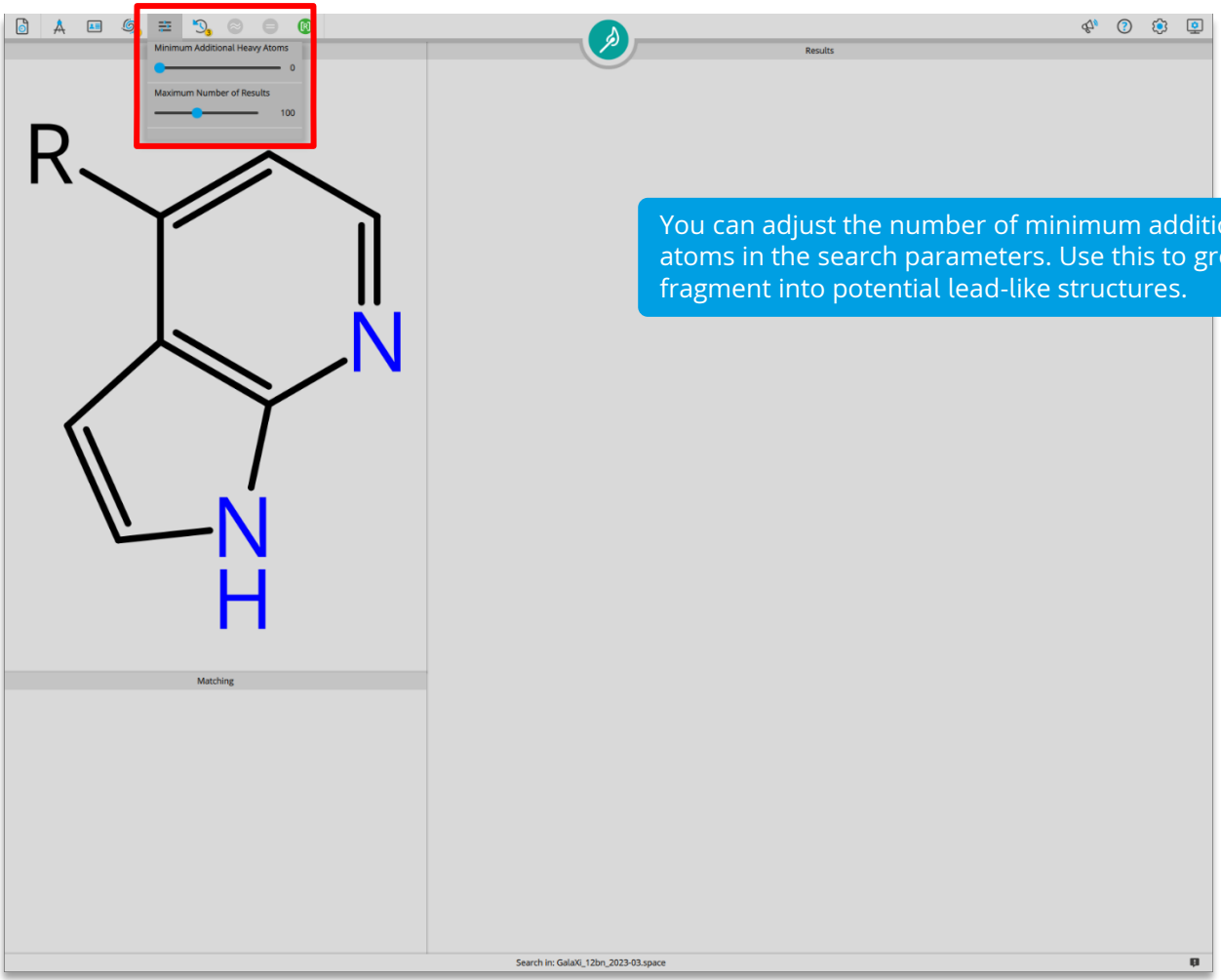
Constraints need to be connected to each other.



To perform an R group search, introduce one or more R definitions via eSeeSketch. The R defines positions of the molecule, where the retrieved results will contain at least one additional heavy atom.
The rest of the molecule will remain unchanged.

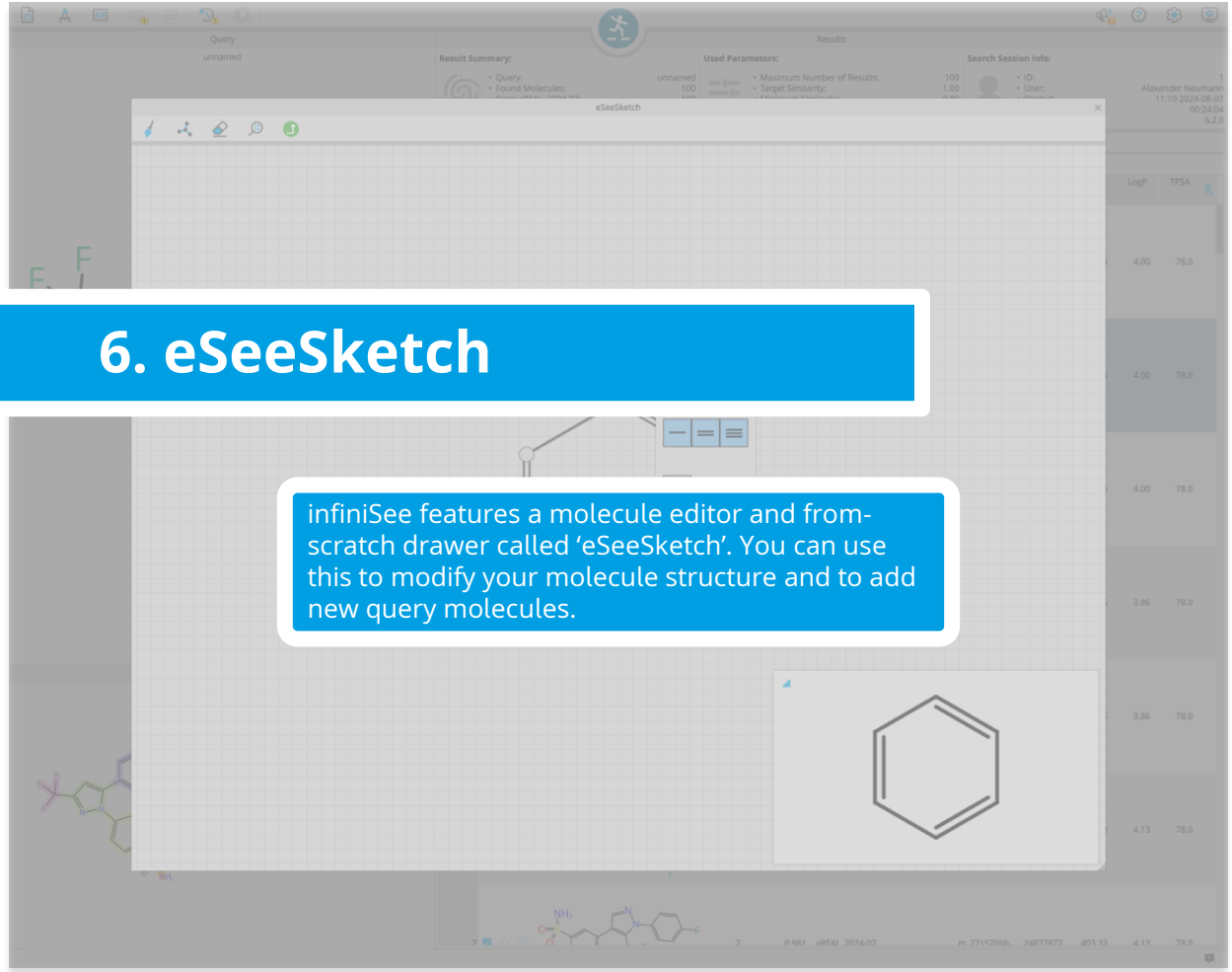


The retrieved results will contain decorations only in the desired positions.

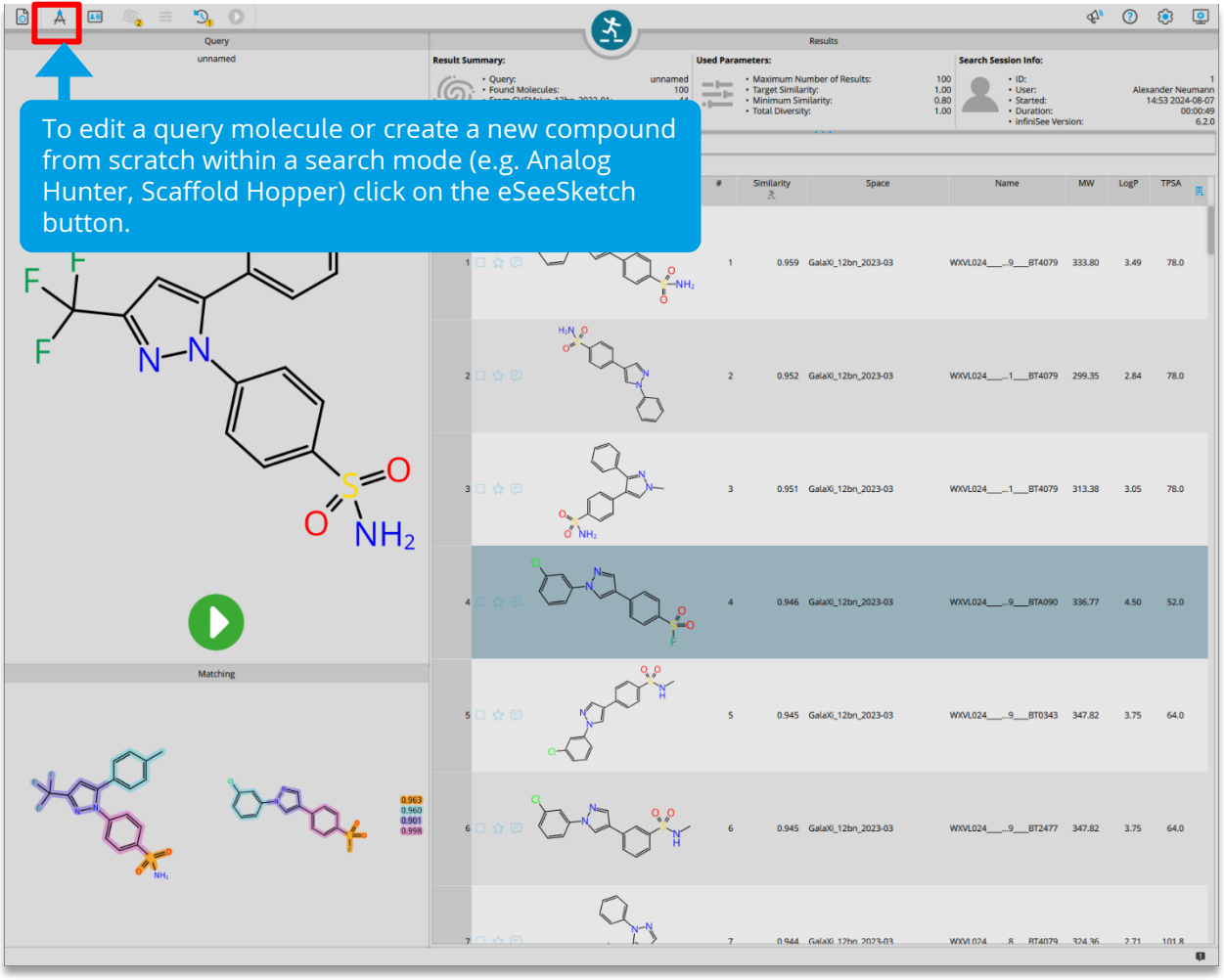


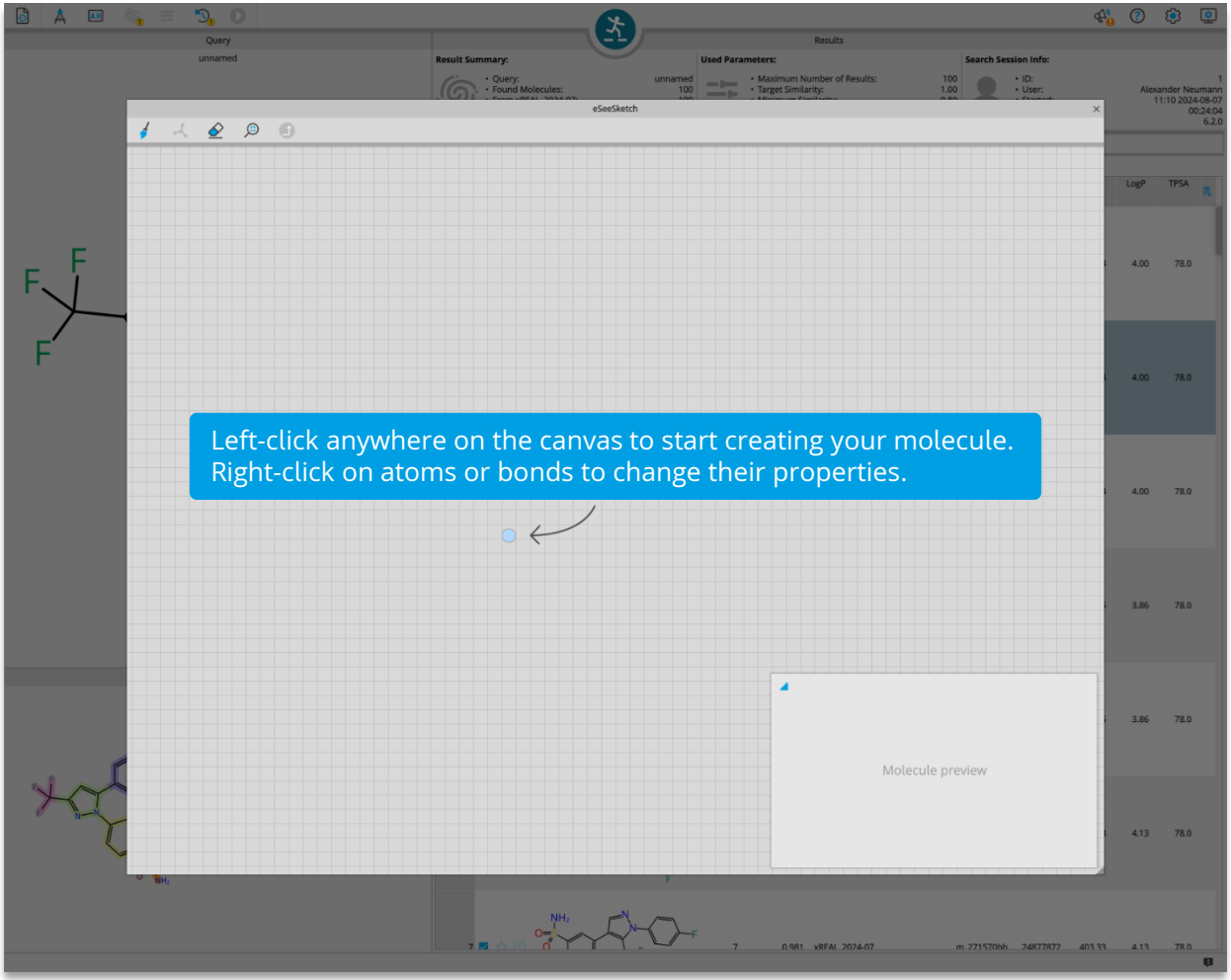
You can adjust the number of minimum additional heavy atoms in the search parameters. Use this to grow your fragment into potential lead-like structures.

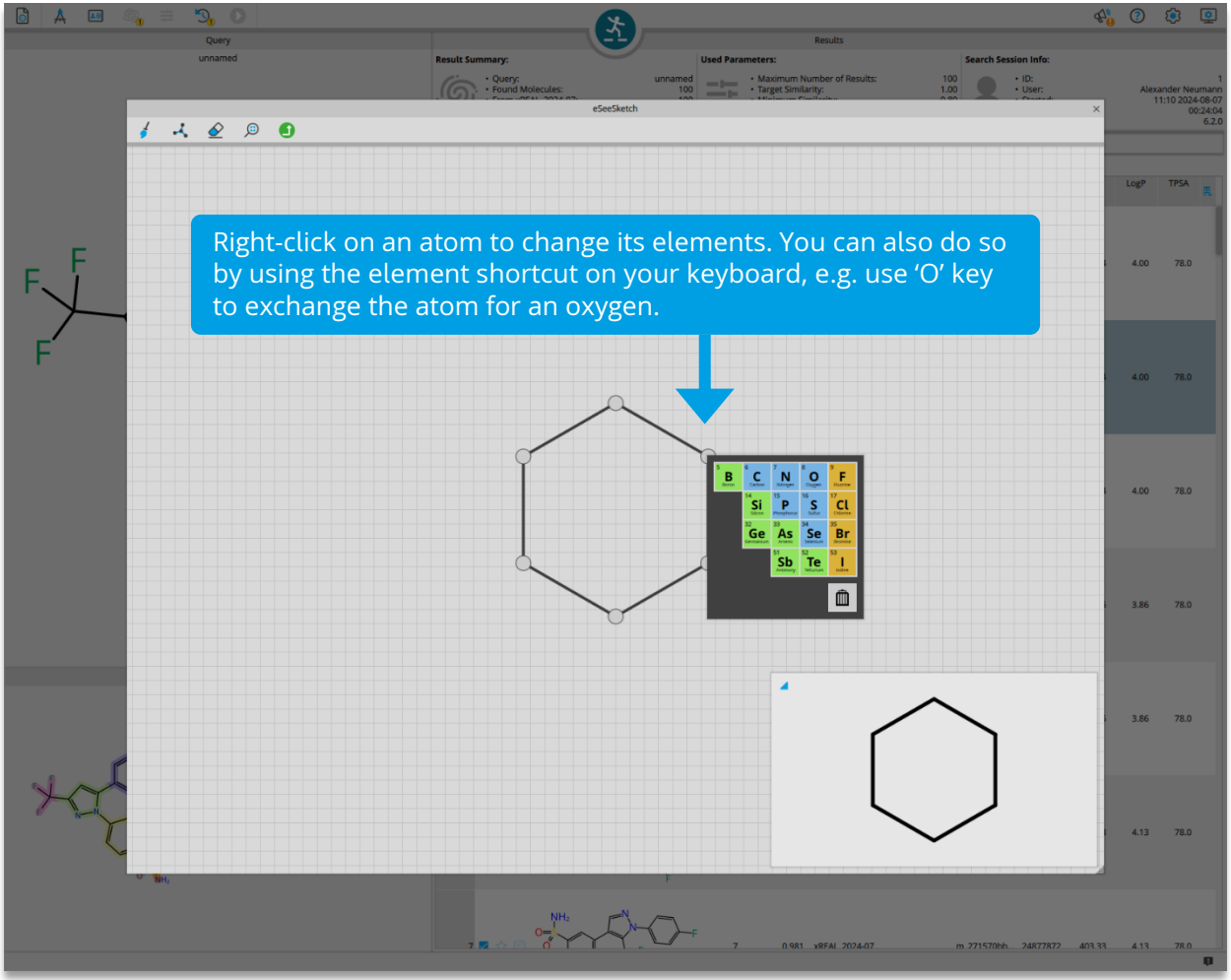
6. eSeeSketch

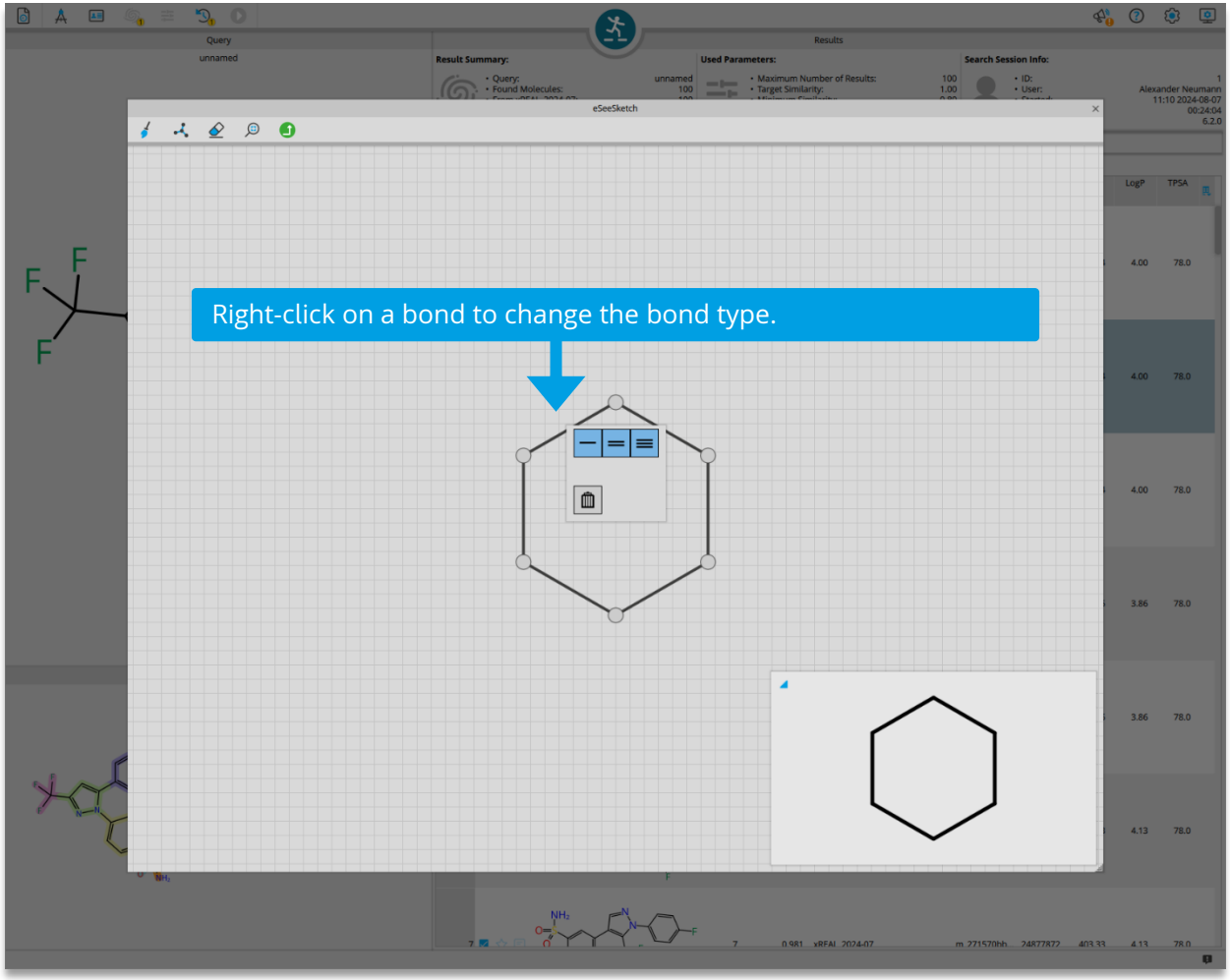


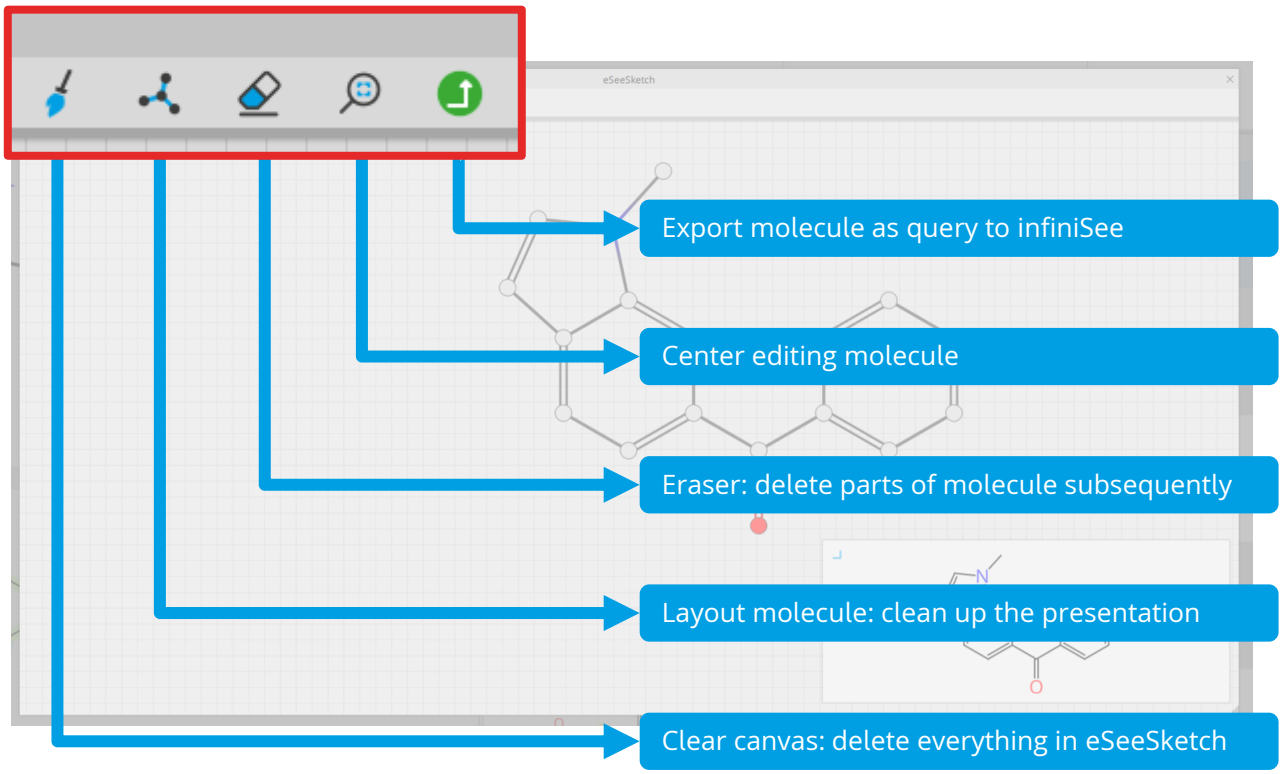
infiniSee features a molecule editor and from-scratch drawer called ‘eSeeSketch’. You can use this to modify your molecule structure and to add new query molecules.

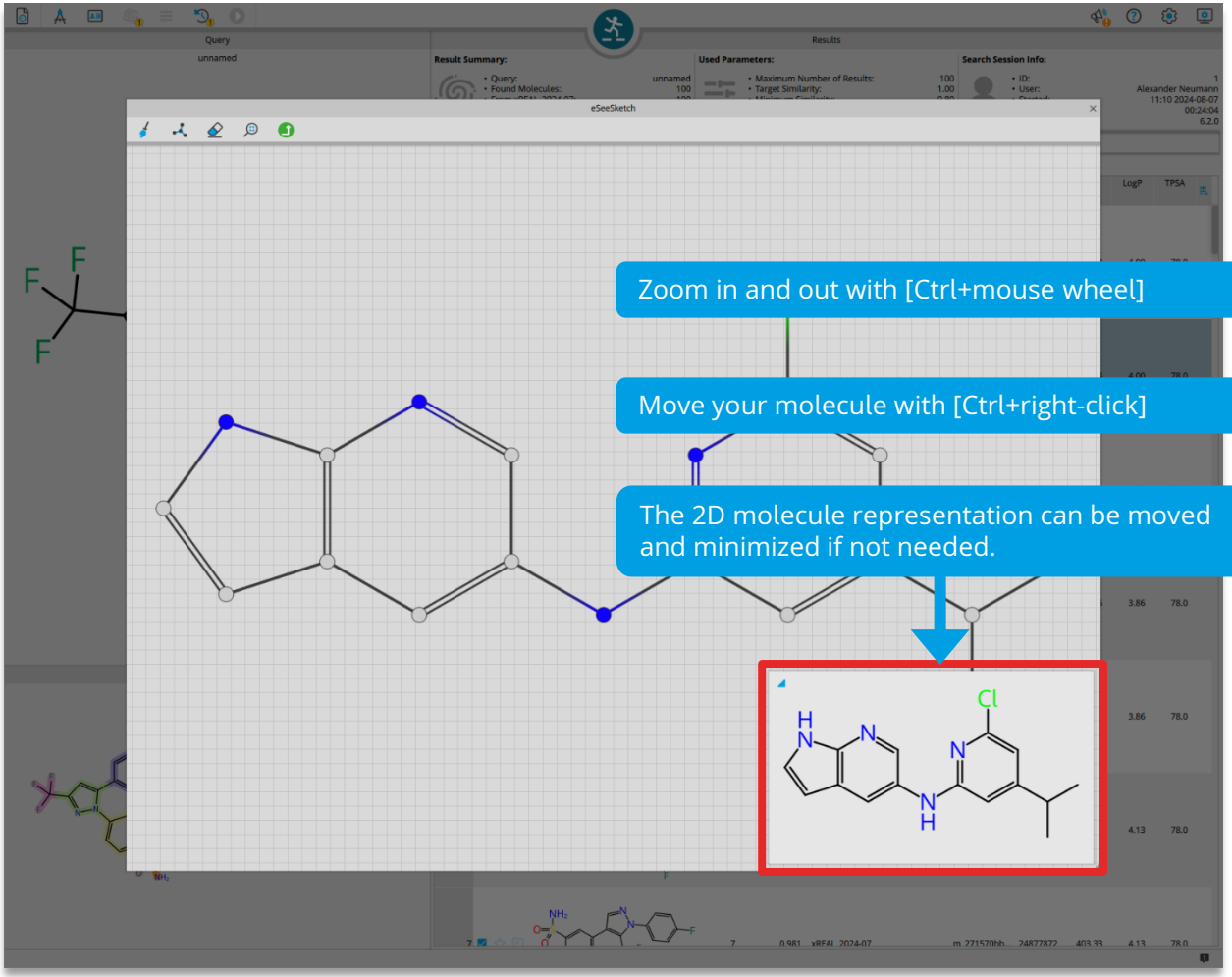

To edit a query molecule or create a new compound from scratch within a search mode (e.g. Analog Hunter, Scaffold Hopper) click on the eSeeSketch button.
Query
unnamed
Results
Result Summary:
Used Parameters:
Search Session Info:
Matching


eSeeSketch
Left-click anywhere on the canvas to start creating your molecule.
Right-click on atoms or bonds to change their properties.
Molecule preview
Results
Result Summary:
Used Parameters:
Search Session Info:
LogP
TPSA


eSeeSketch
Right-click on an atom to change its elements. You can also do so by using the element shortcut on your keyboard, e.g. use ‘O’ key to exchange the atom for an oxygen.
B C N O F
Si P S Cl
Ge As Se Br
Sb Te I


eSeeSketch
Right-click on a bond to change the bond type.


Export molecule as query to infiniSee
Center editing molecule
Eraser: delete parts of molecule subsequently
Layout molecule: clean up the presentation
Clear canvas: delete everything in eSeeSketch


Zoom in and out with [Ctrl+mouse wheel]
Move your molecule with [Ctrl+right-click]
The 2D molecule representation can be moved and minimized if not needed.

Set sail and discover unlimited accessibles with infiniSee.

If you have any problems, please reach out to us:
support@biosolveit.de