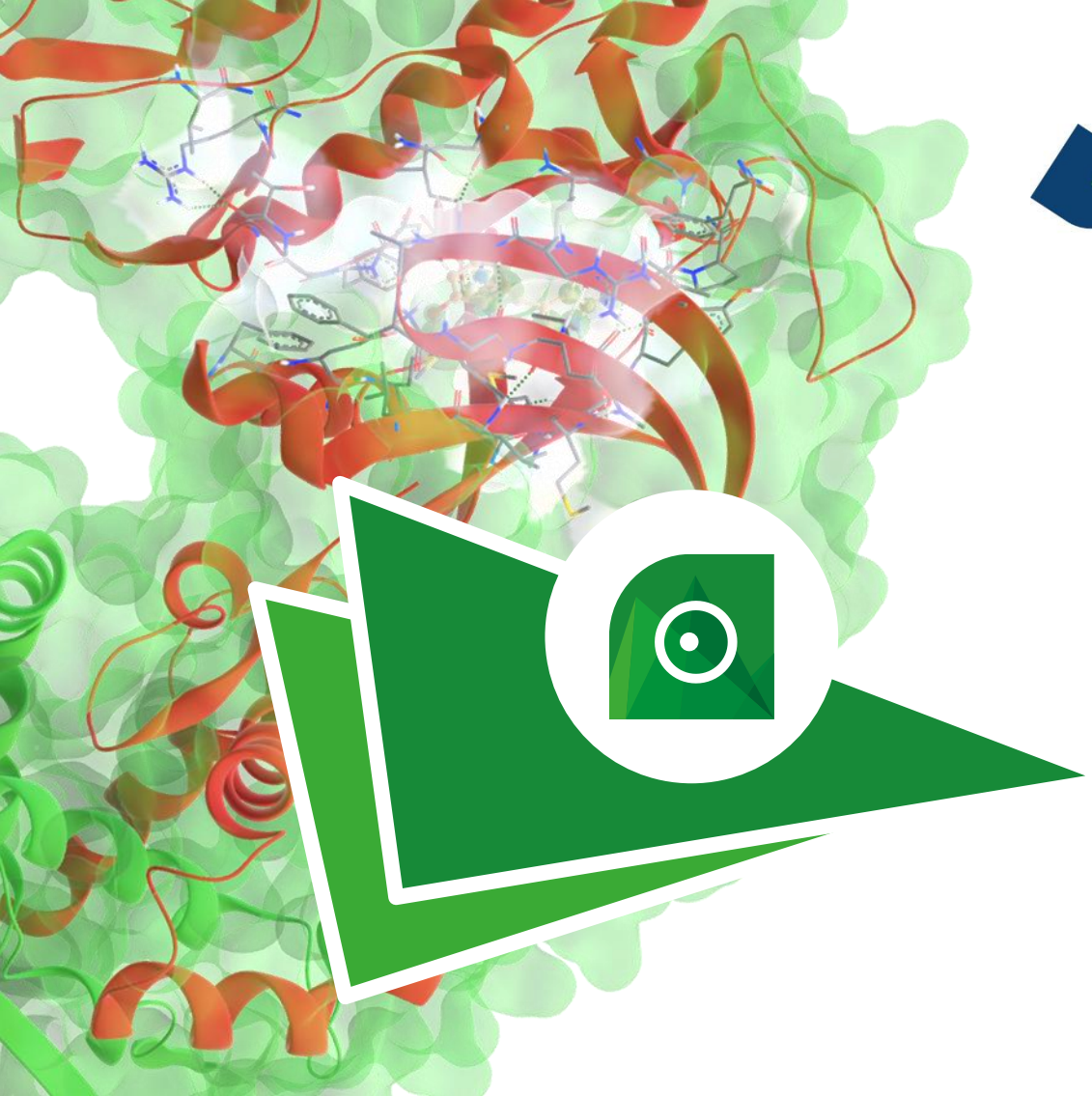


BioSolveIT
expect actives!

SeeSAR

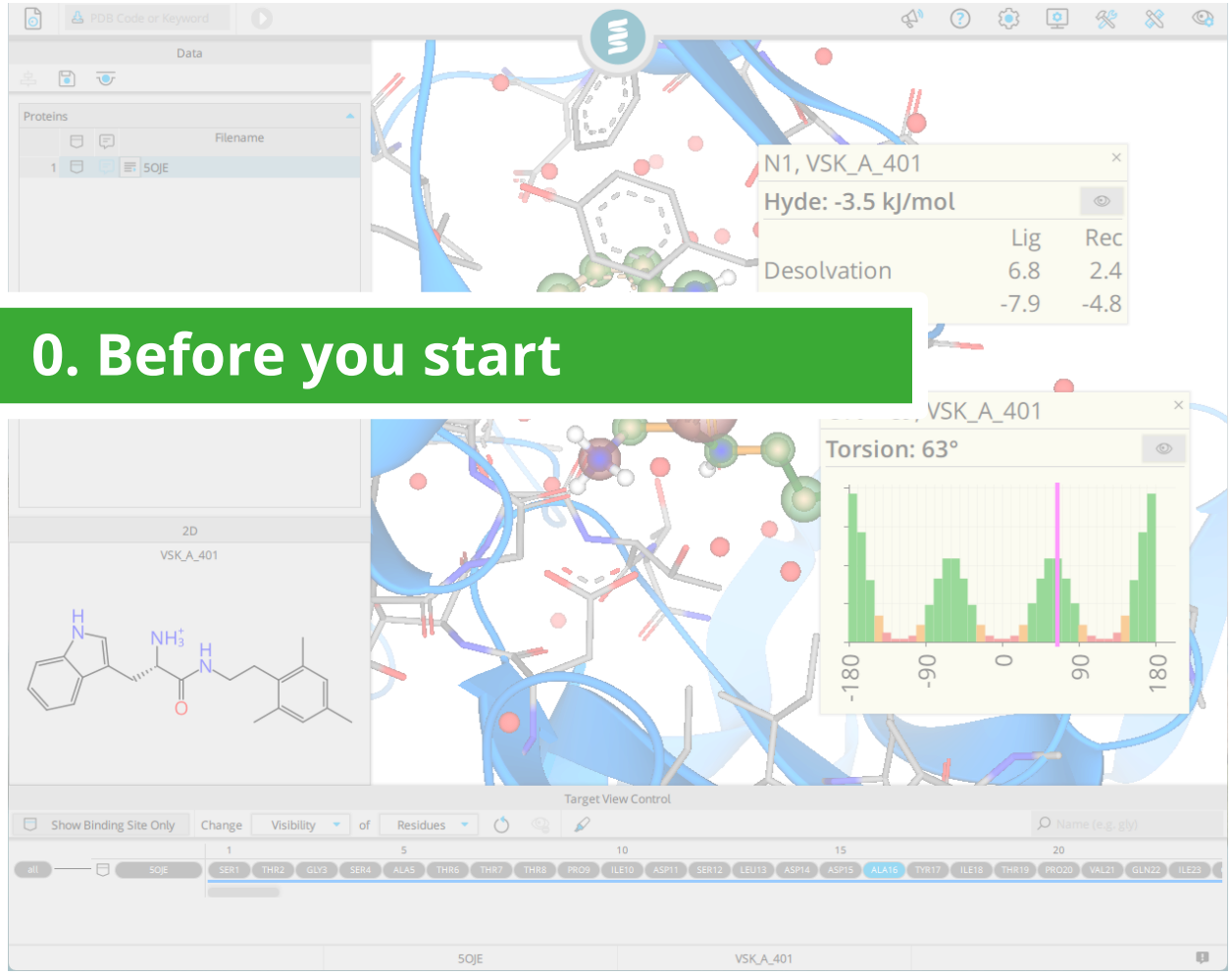
Beginner's Guide
Version 14 - Atlas

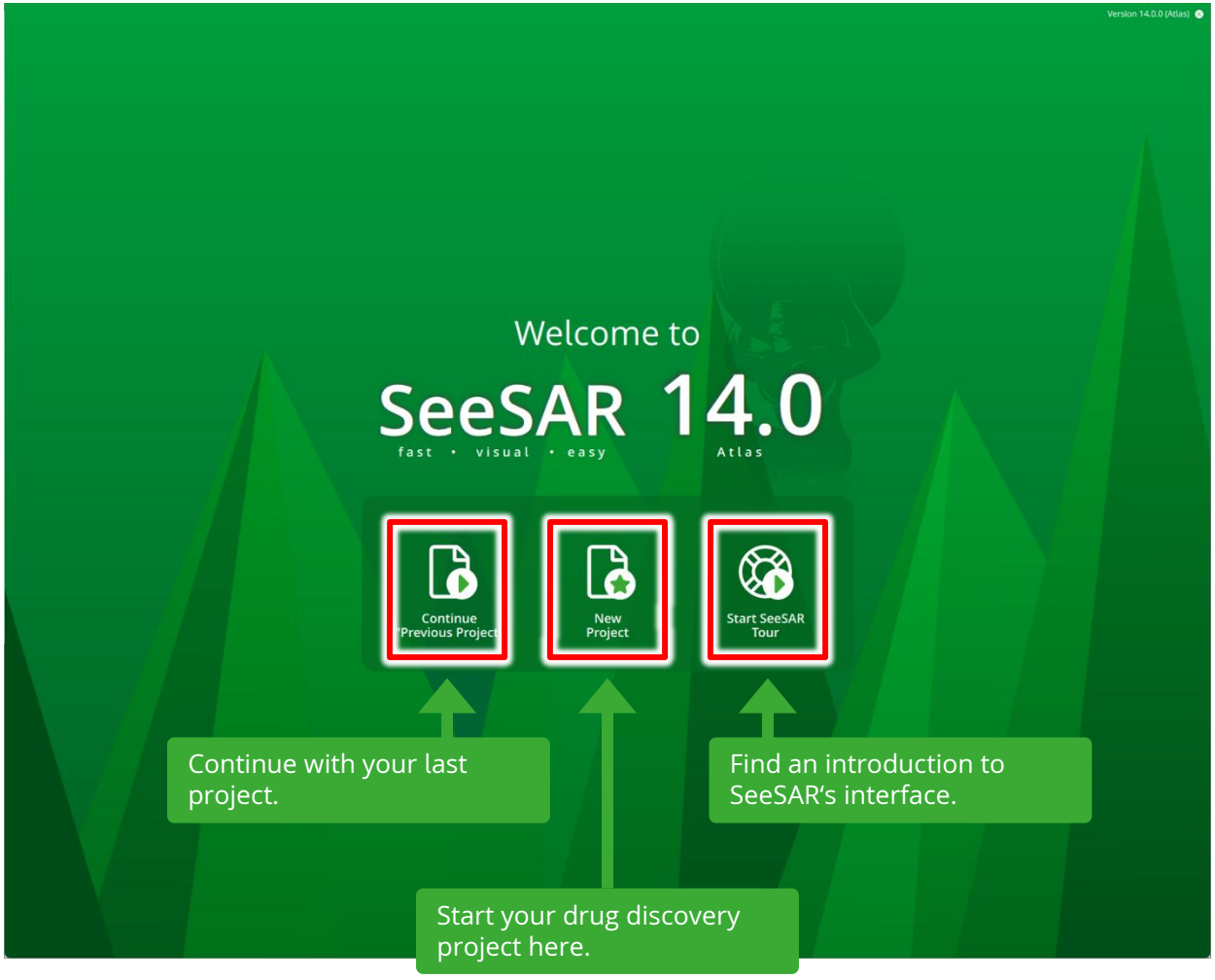
Time to start an interactive dialog with your compound!

Click on the section you are interested in

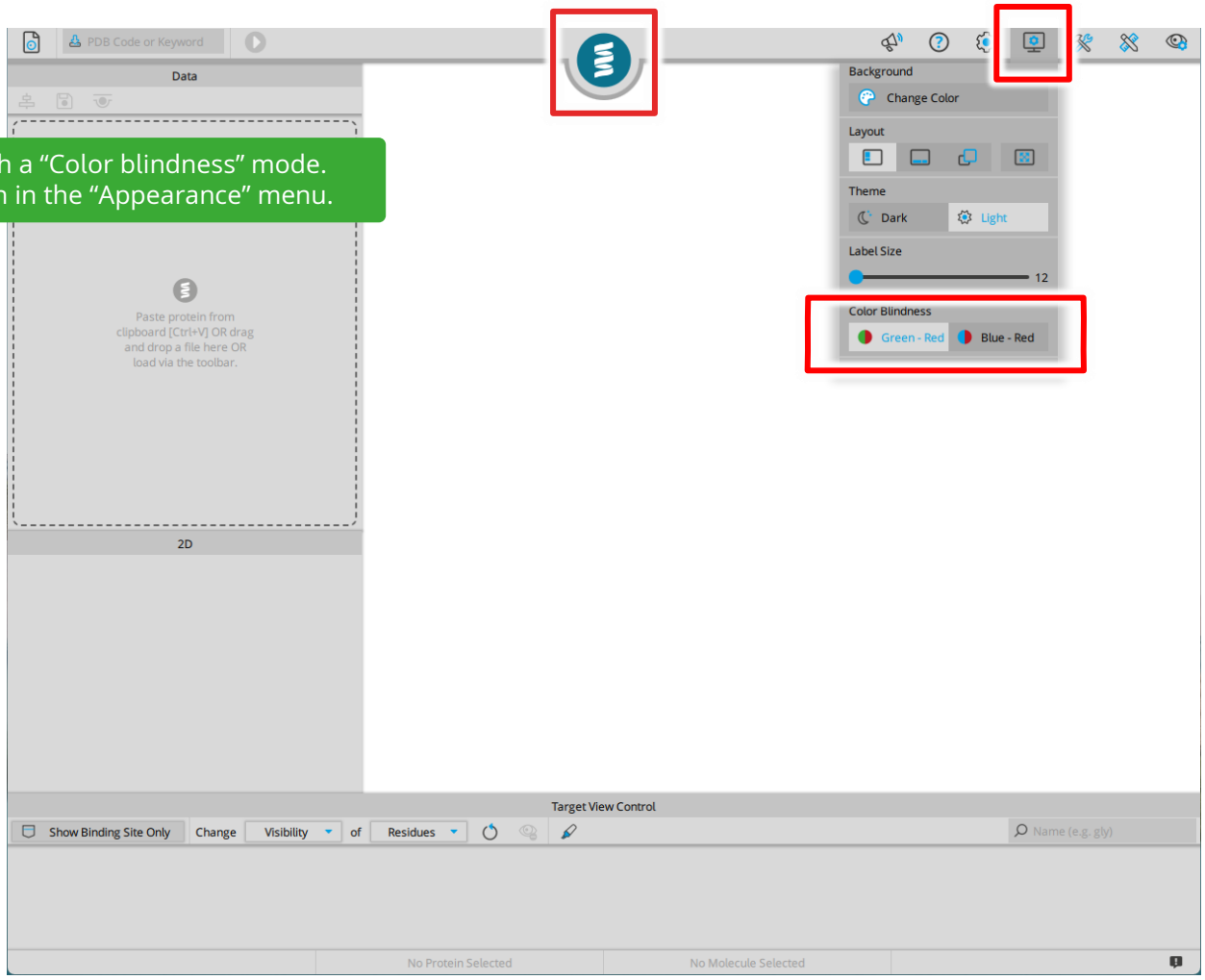
Content

0. Before you start

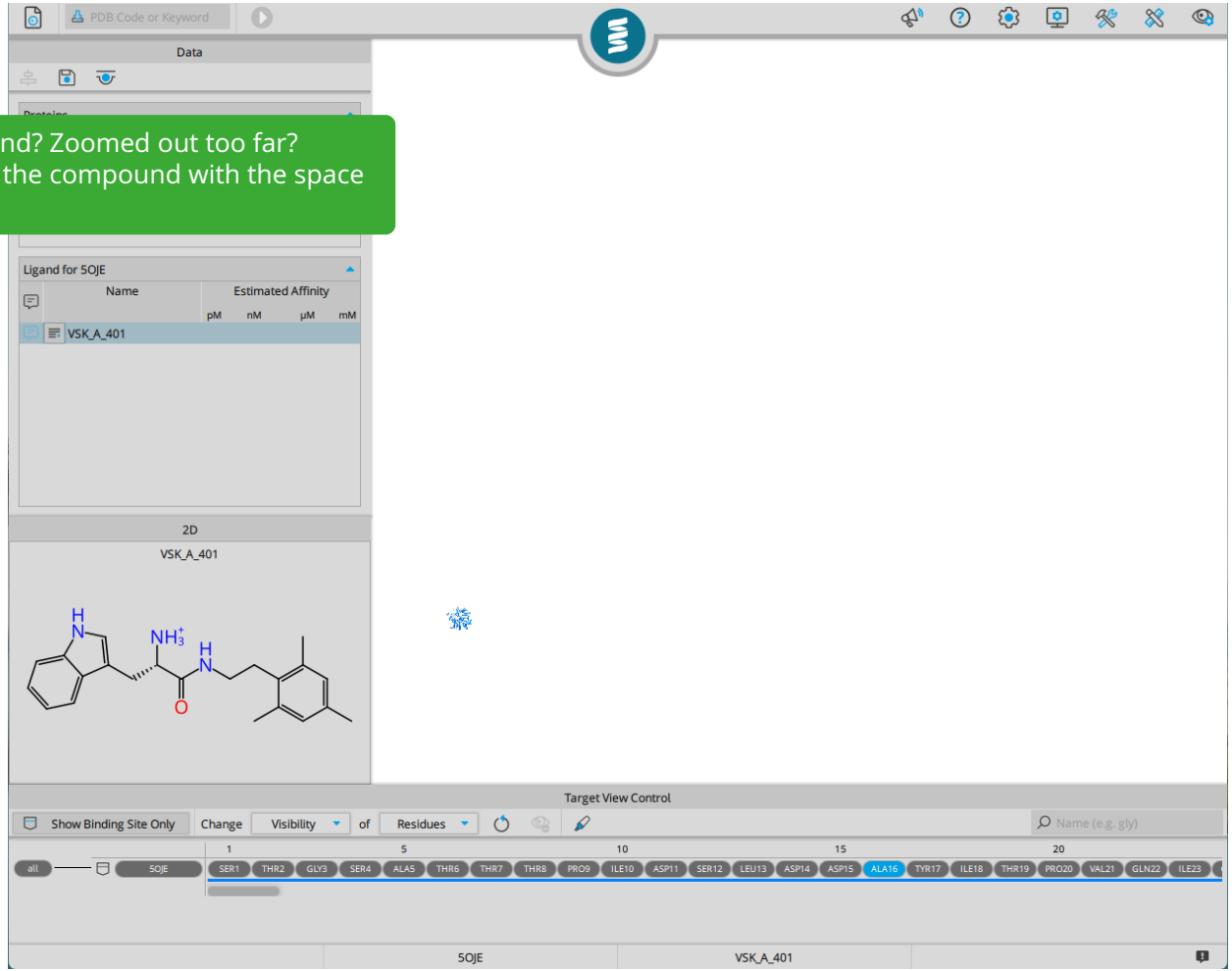



Version 14.0.0 (Atlas)
Welcome to
SeeSAR 14.0
fast • visual • easy
Atlas
Continue Previous Project
New Project
Start SeeSAR Tour
Continue with your last project.
Start your drug discovery project here.
Find an introduction to SeeSAR's interface.

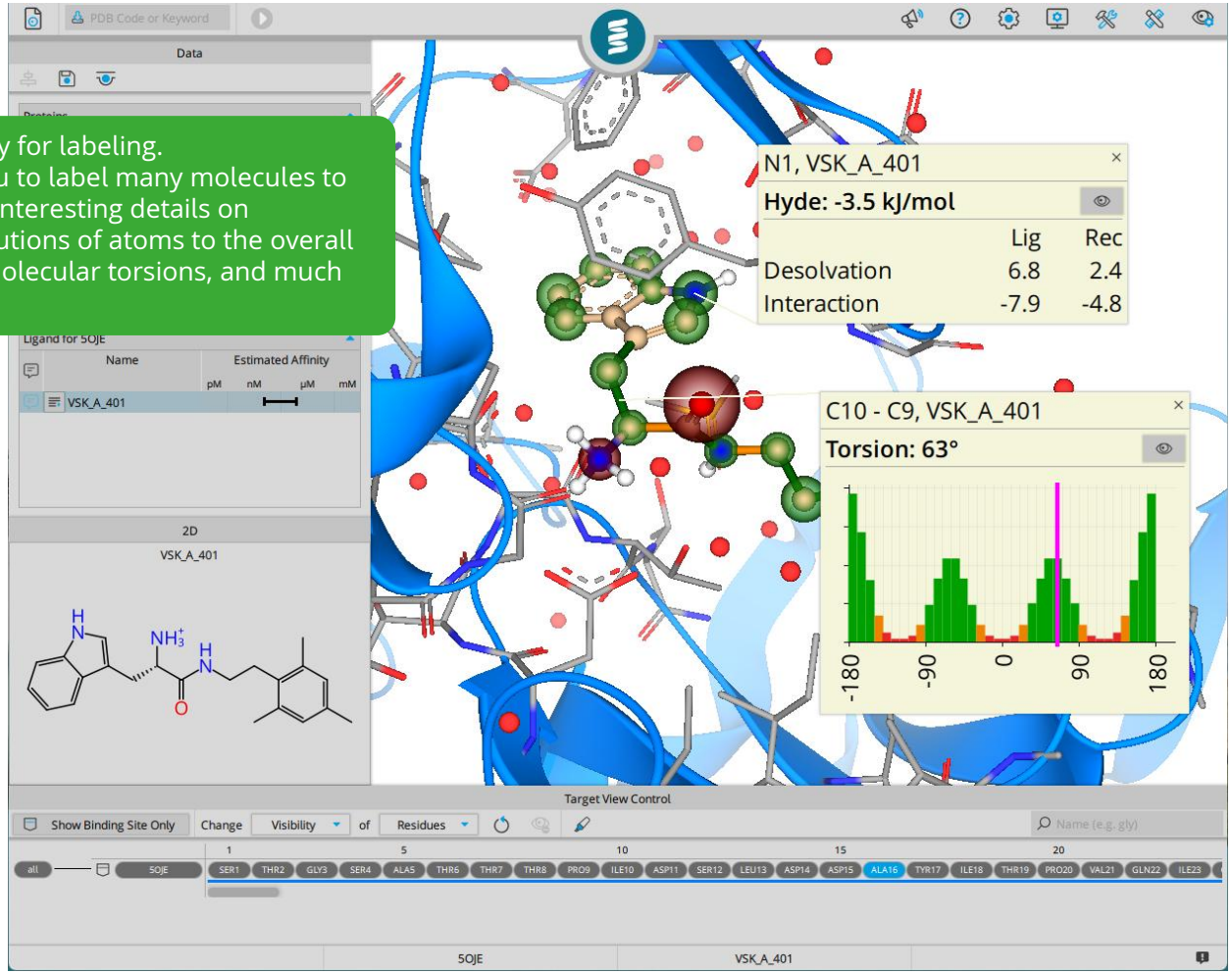
SeeSAR comes with a “Color blindness” mode.
It can be turned on in the “Appearance” menu.



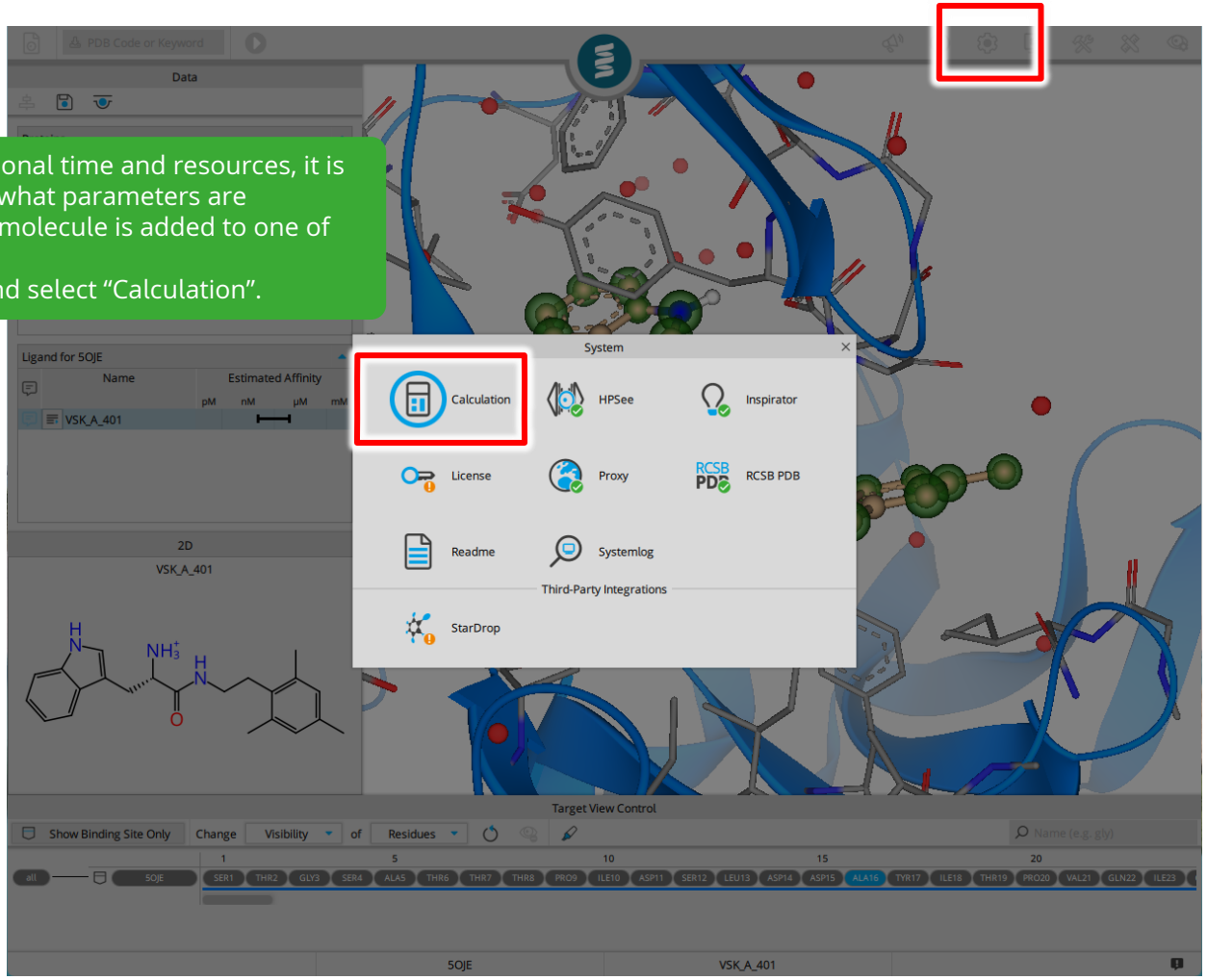
Lost your compound? Zoomed out too far? Focus the view on the compound with the space bar.



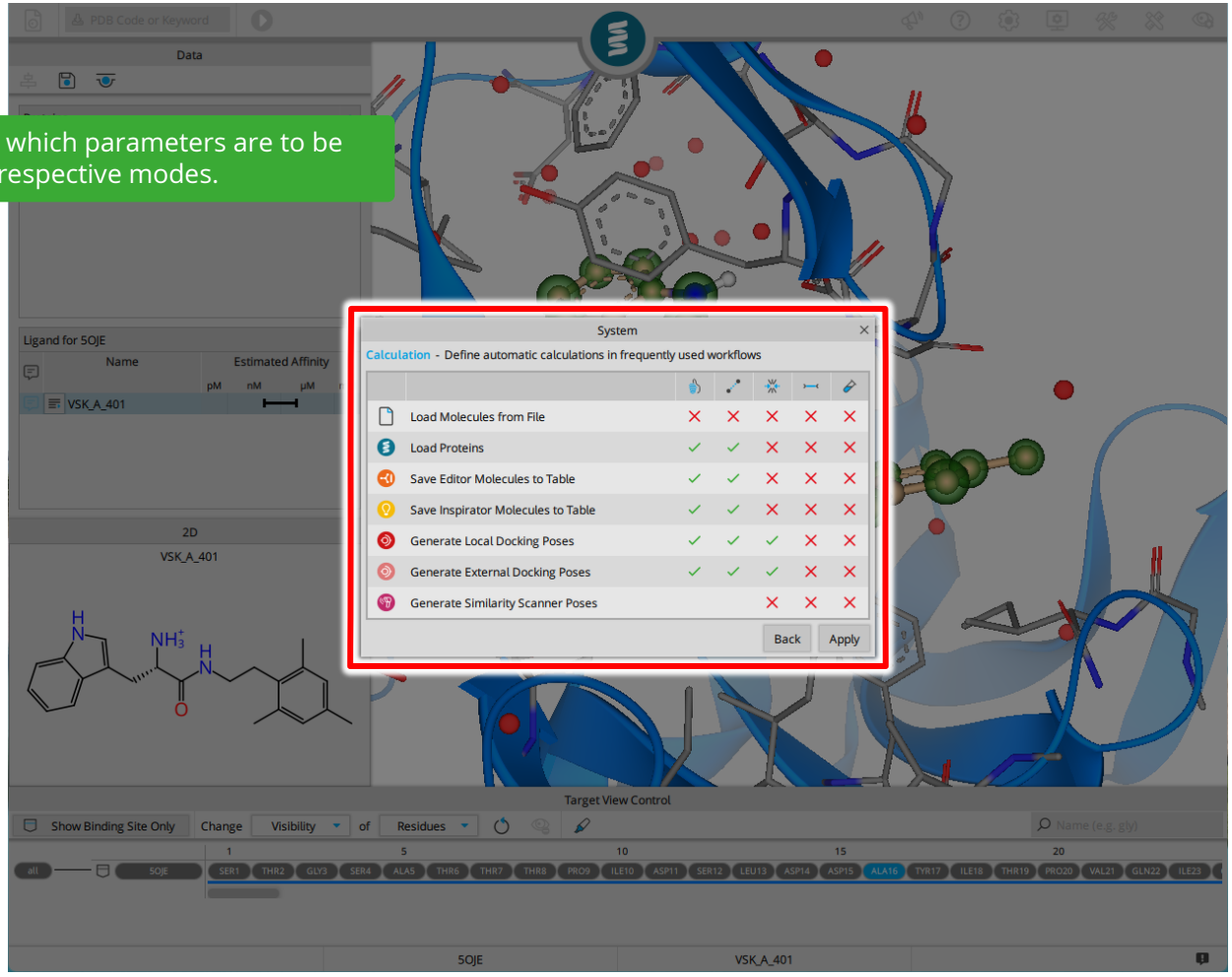
Use the “L” hot key for labeling.
SeeSAR allows you to label many molecules to provide you with interesting details on individual contributions of atoms to the overall binding affinity, molecular torsions, and much more.

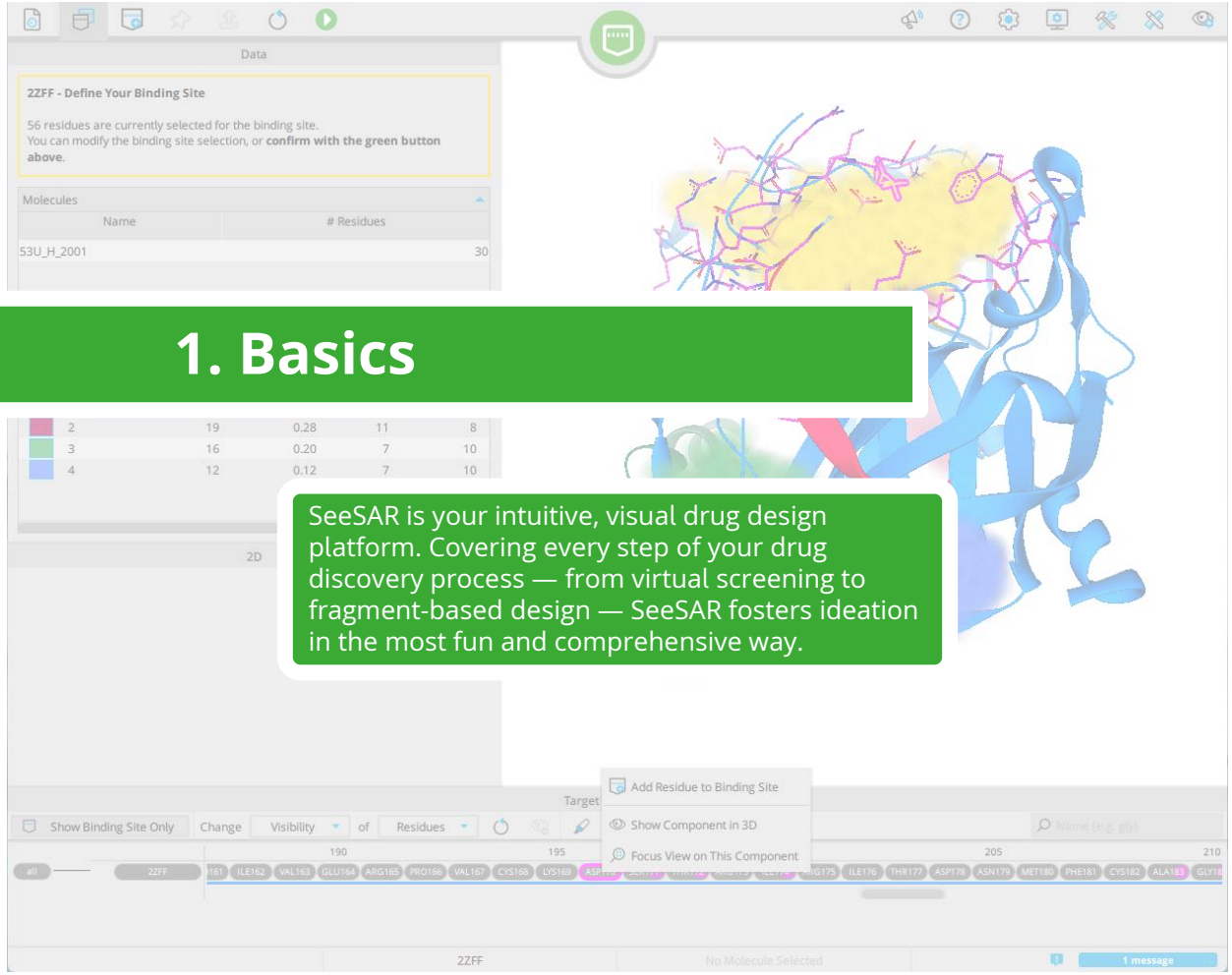


To save computational time and resources, it is possible to select what parameters are calculated once a molecule is added to one of SeeSAR'S modes.
Got to "System" and select "Calculation".



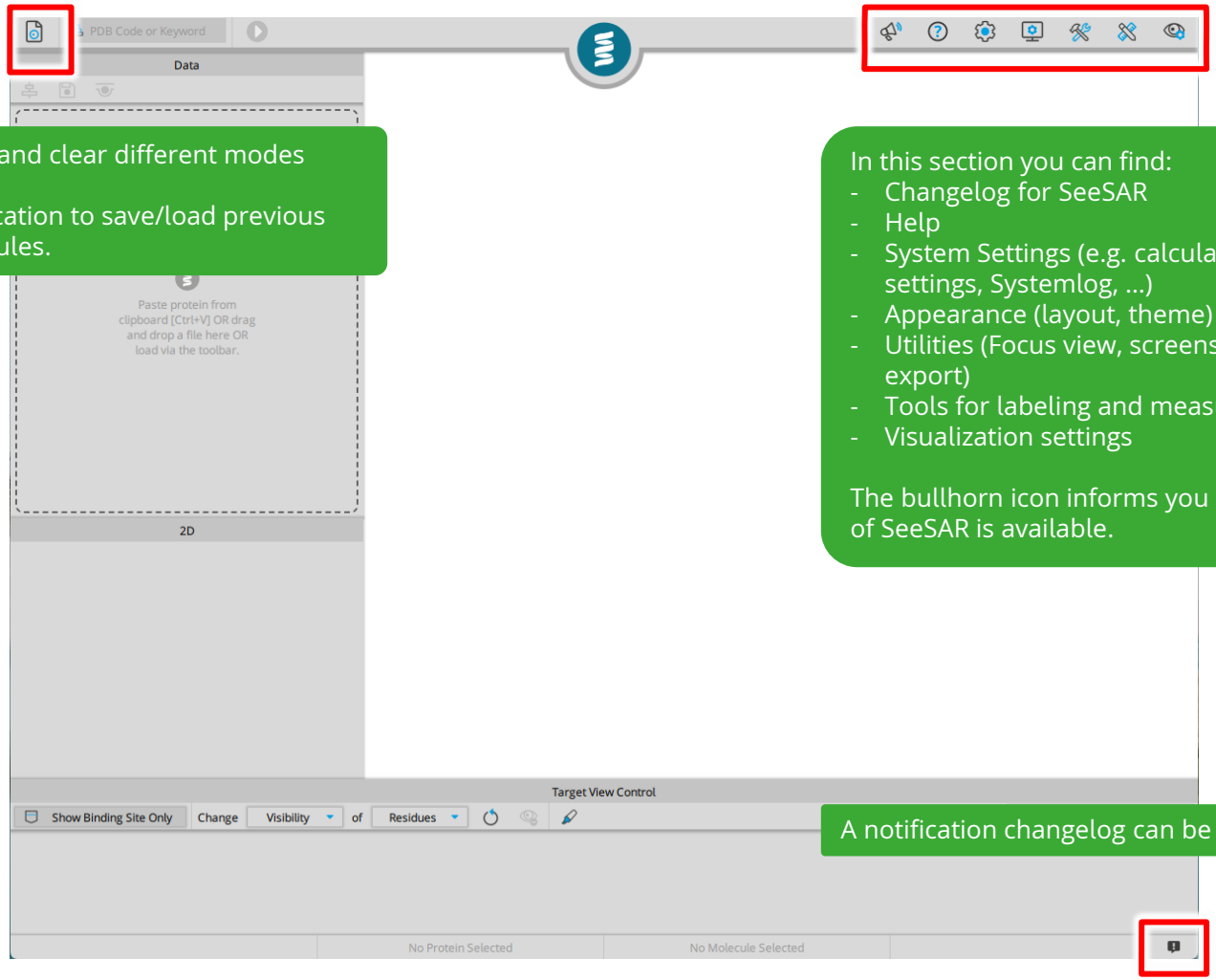
In the table, select which parameters are to be calculated for the respective modes.





1. Basics

SeeSAR is your intuitive, visual drug design platform. Covering every step of your drug discovery process — from virtual screening to fragment-based design — SeeSAR fosters ideation in the most fun and comprehensive way.

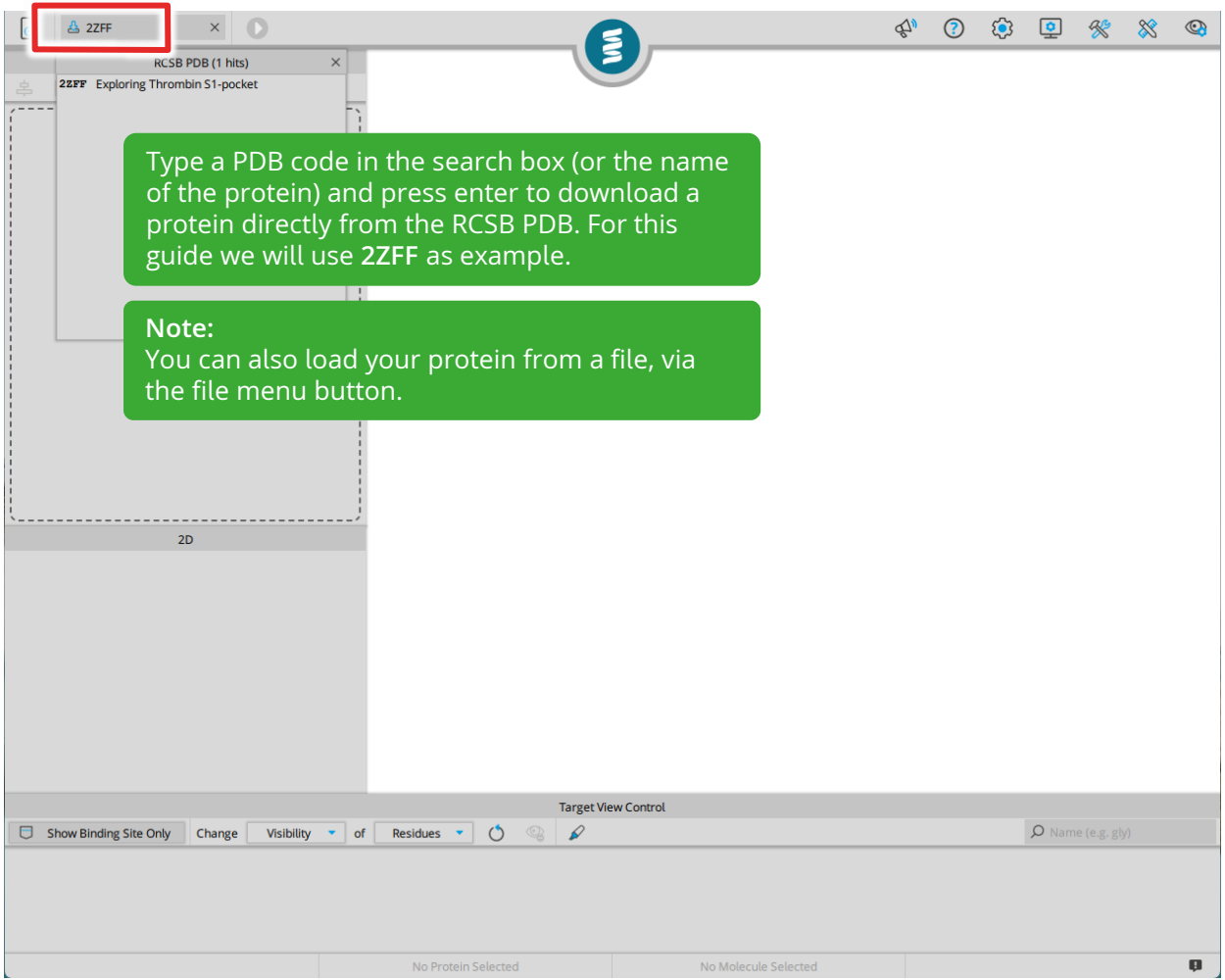


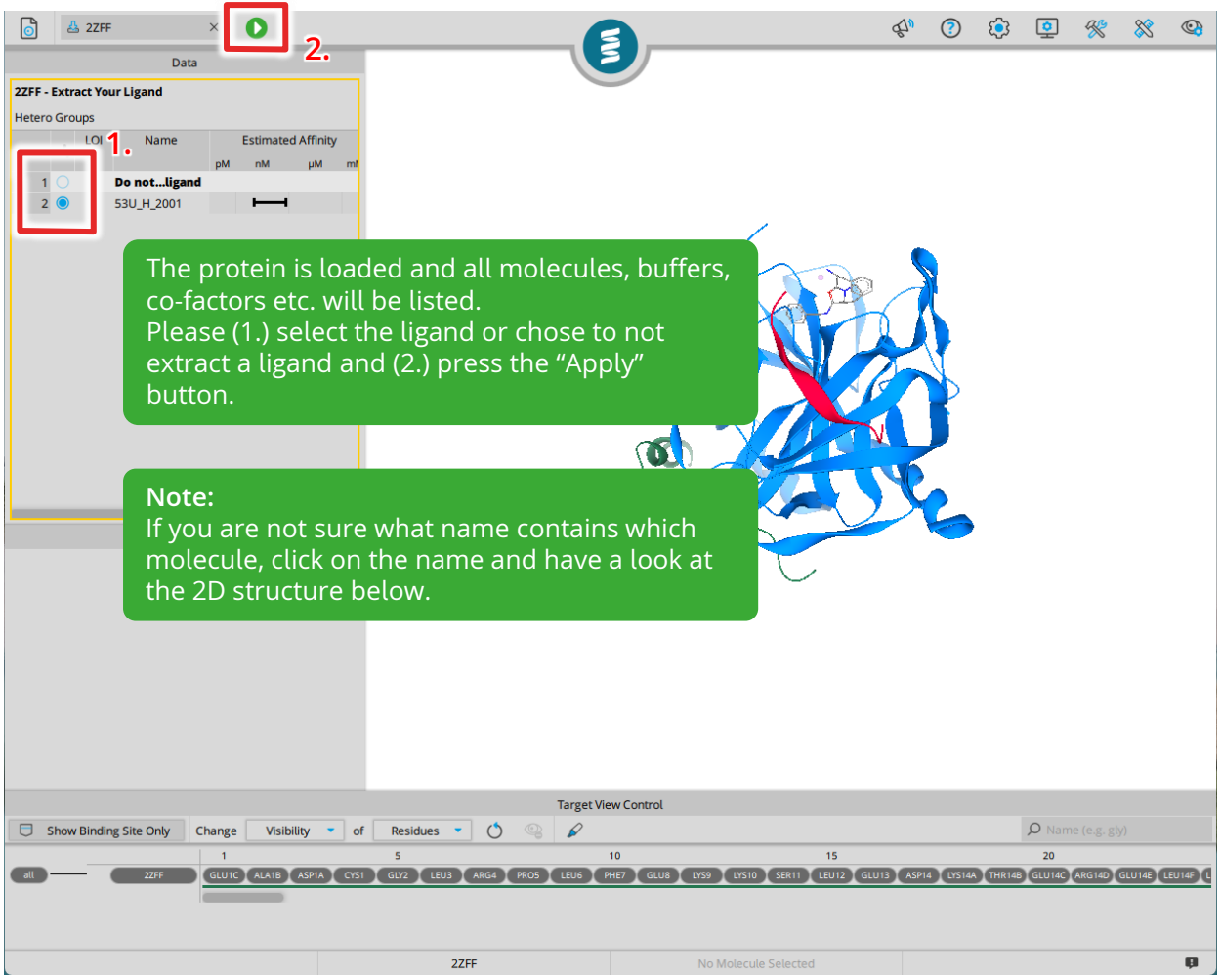
Start new project and clear different modes here.
This is also the location to save/load previous projects or molecules.

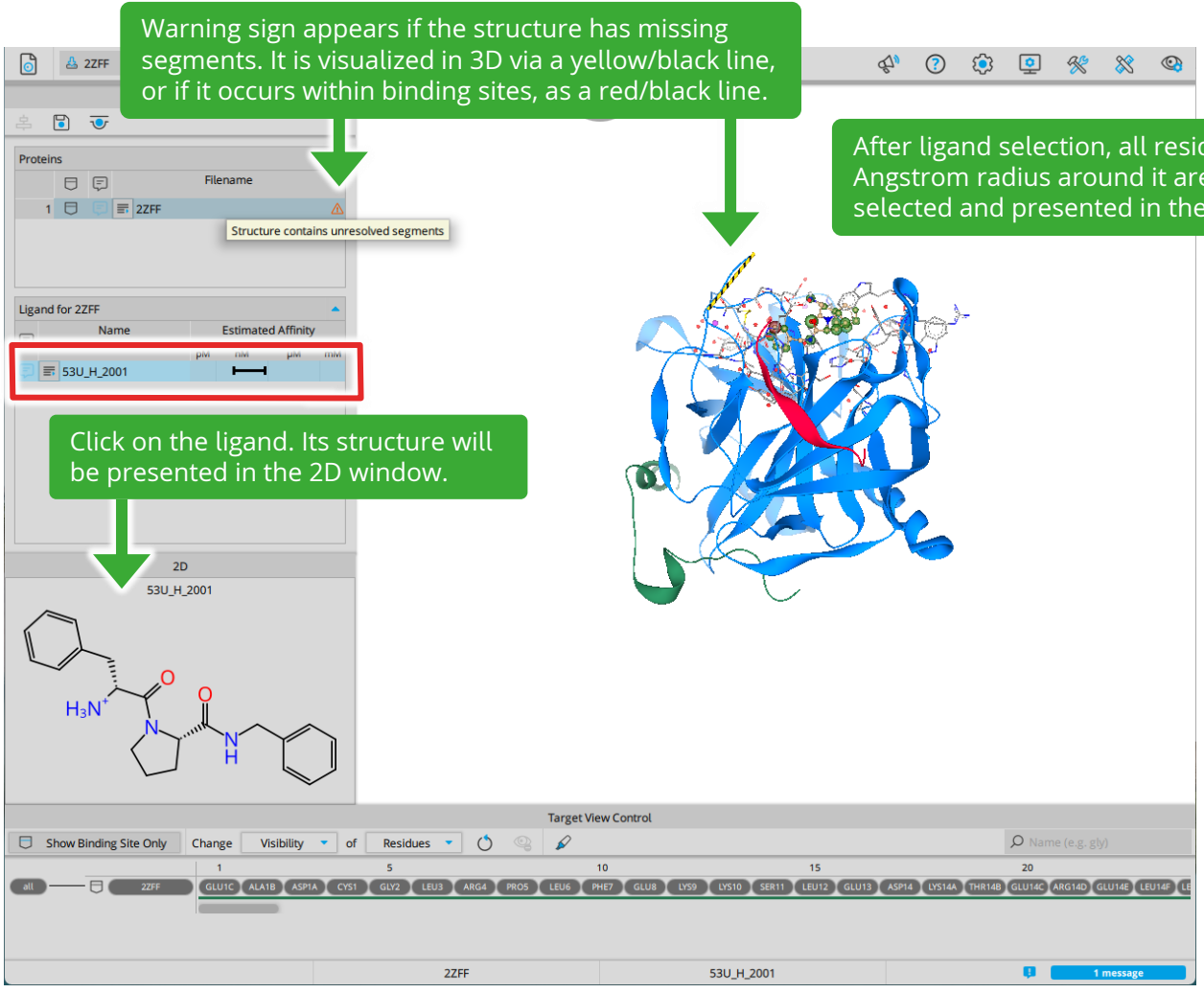
In this section you can find:
- Changelog for SeeSAR
- Help
- System Settings (e.g. calculations, license settings, Systemlog, ...)
- Appearance (layout, theme)
- Utilities (Focus view, screenshots, 3D scene export)
- Tools for labeling and measurement
- Visualization settings

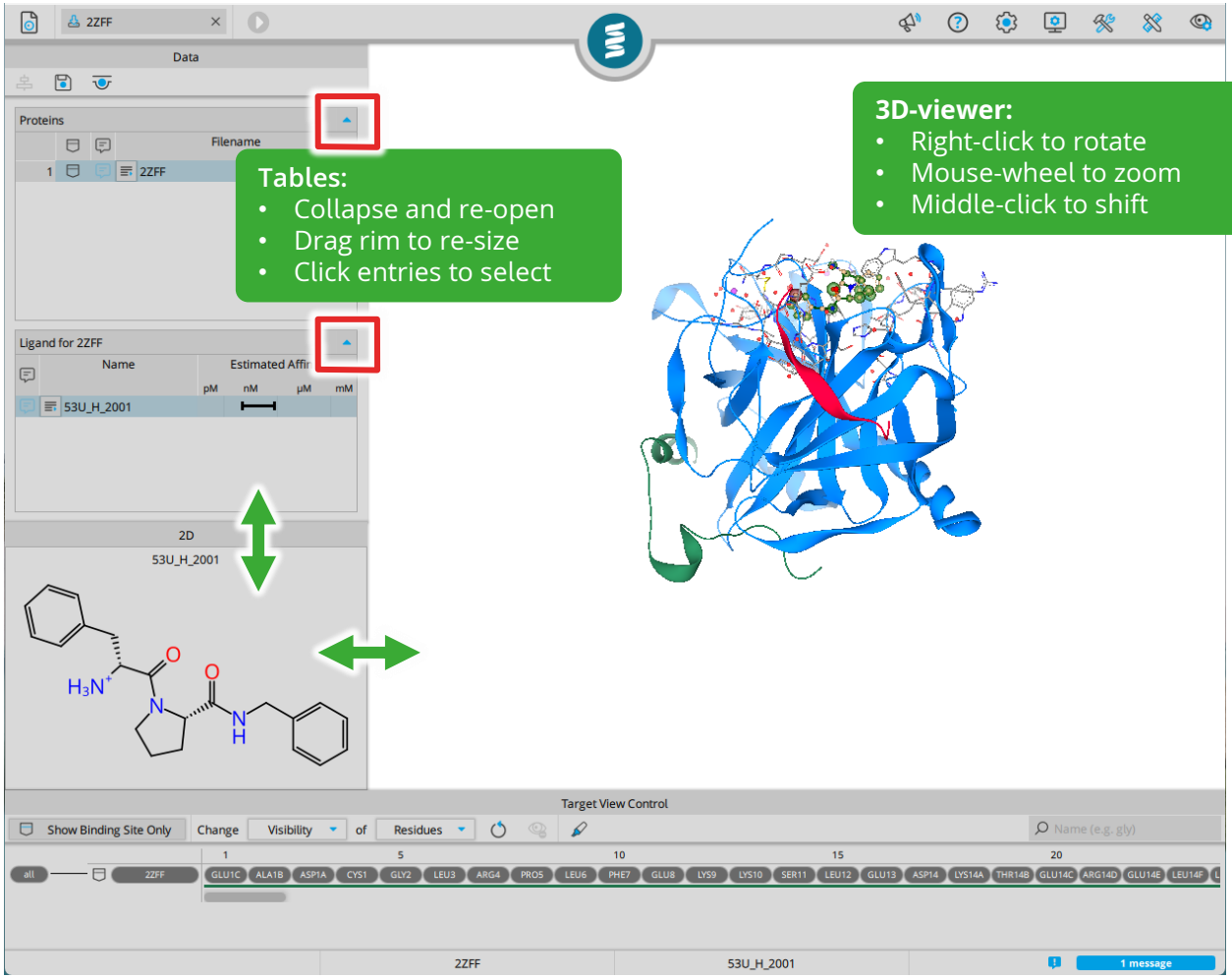
The bullhorn icon informs you if a new version of SeeSAR is available.

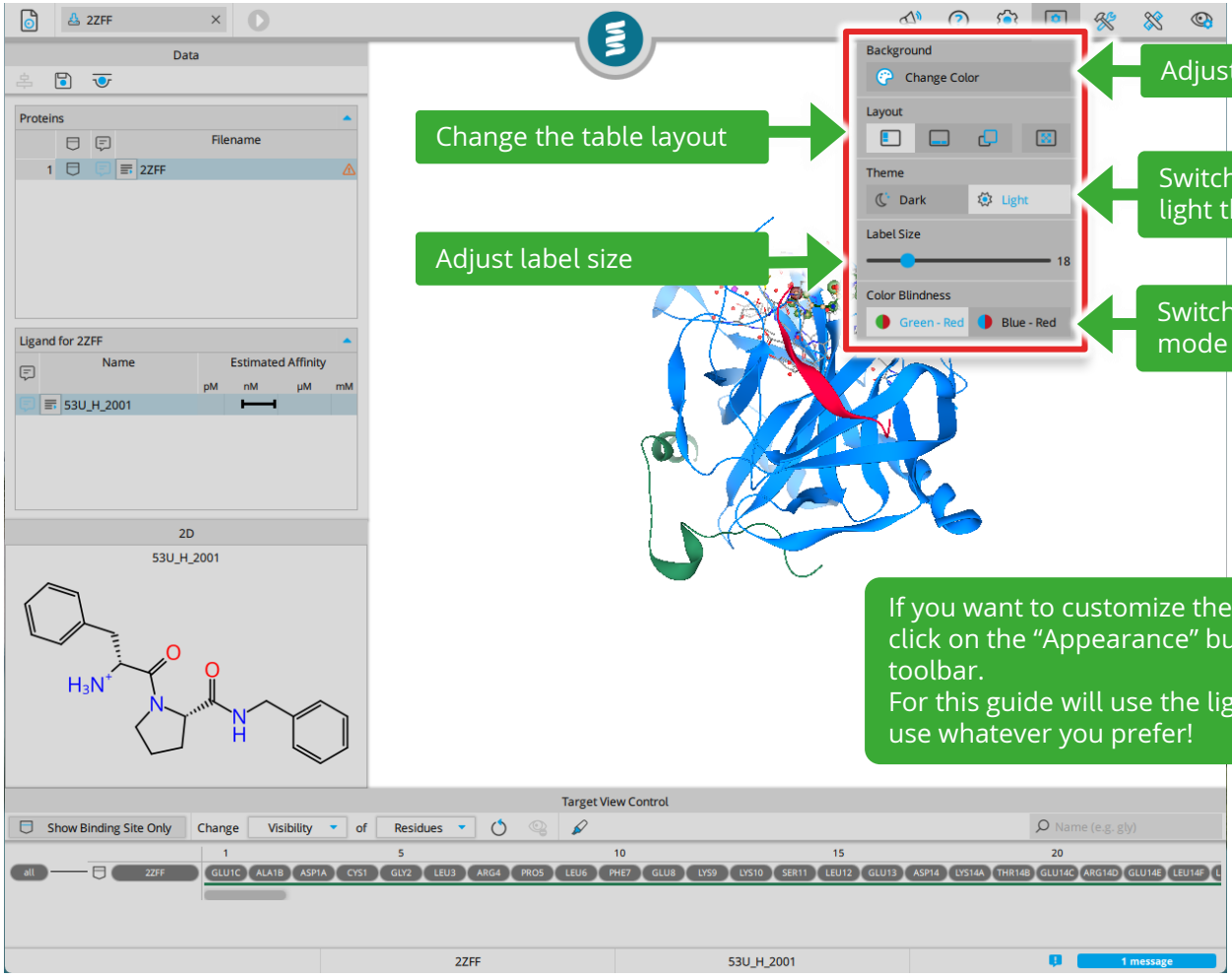
A notification changelog can be found here.

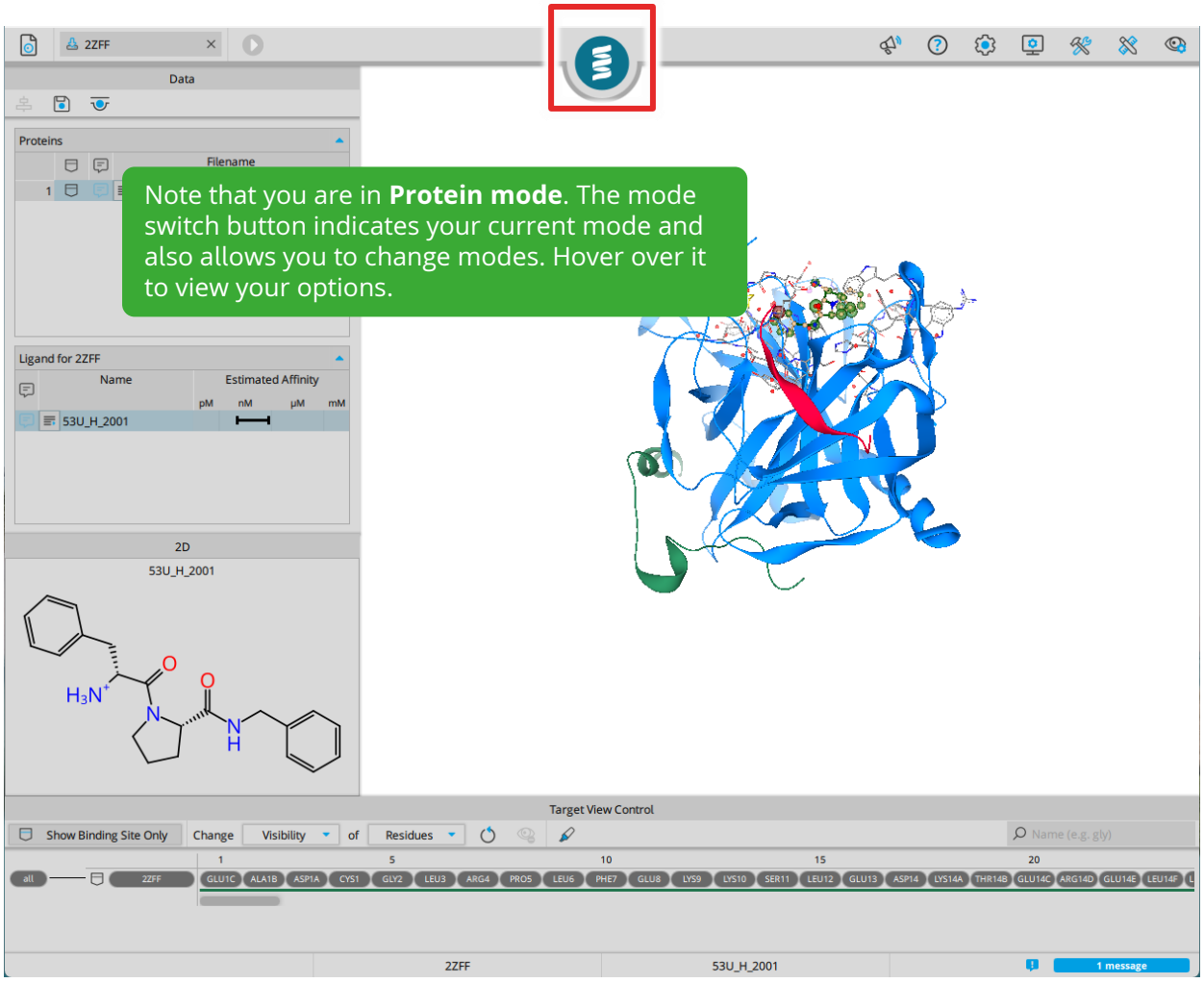

2ZFF
RCSB PDB (1 hits)
2ZFF Exploring Thrombin S1-pocket
2D
Type a PDB code in the search box (or the name of the protein) and press enter to download a protein directly from the RCSB PDB. For this guide we will use 2ZFF as example.
Note:
You can also load your protein from a file, via the file menu button.
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
Name (e.g. gly)
No Protein Selected
No Molecule Selected

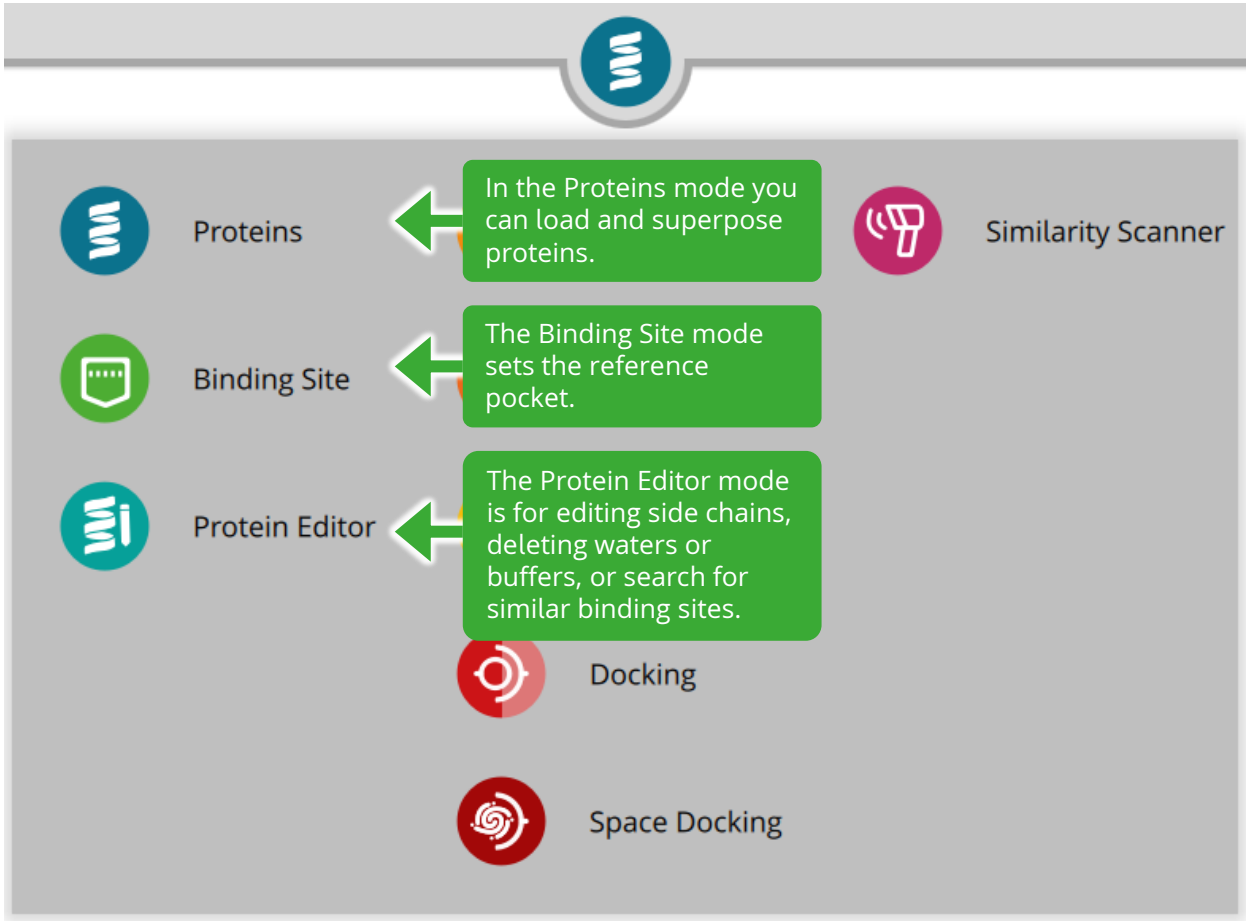

2ZFF
2.
Data
2ZFF - Extract Your Ligand
Hetero Groups
LOI
Name
Estimated Affinity
pM
nM
µM
1.
1
Do not...ligand
2
53U_H_2001
The protein is loaded and all molecules, buffers, co-factors etc. will be listed.
Please (1.) select the ligand or chose to not extract a ligand and (2.) press the “Apply” button.
Note:
If you are not sure what name contains which molecule, click on the name and have a look at the 2D structure below.
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
Name (e.g. gly)
all
2ZFF
GLU1C
ALA1B
ASP1A
CYS1
GLY2
LEU3
ARG4
PRO5
LEU6
PHE7
GLU8
LYS9
LYS10
SER11
LEU12
GLU13
ASP14
LYS14A
THR14B
GLU14C
ARG14D
GLU14E
LEU14F
2ZFF
No Molecule Selected

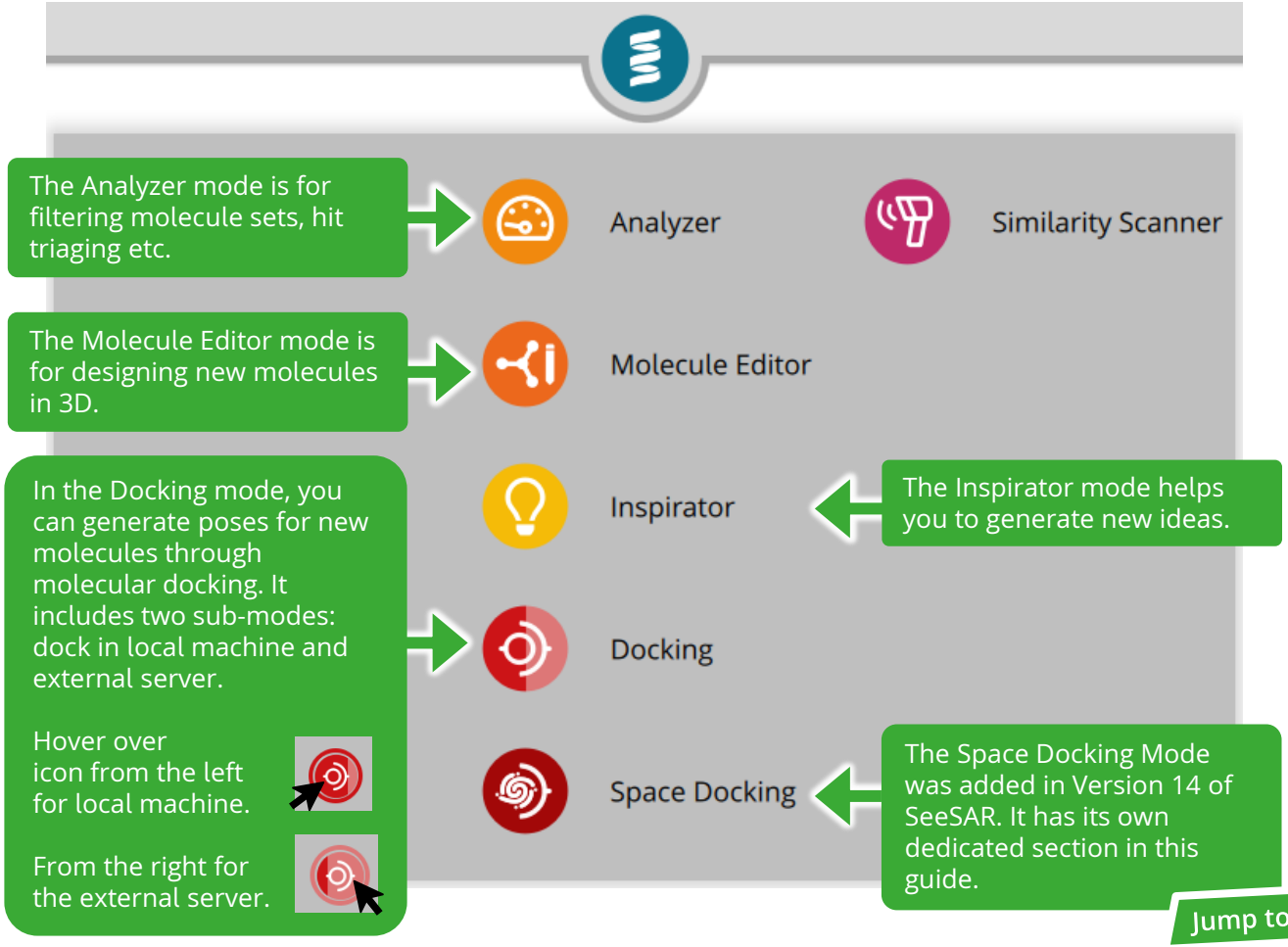

Warning sign appears if the structure has missing segments. It is visualized in 3D via a yellow/black line, or if it occurs within binding sites, as a red/black line.
After ligand selection, all residues within a 6.5 Angstrom radius around it are automatically selected and presented in the model.
Click on the ligand. Its structure will be presented in the 2D window.
2ZFF
Proteins
Filename
1
2ZFF
Structure contains unresolved segments
Ligand for 2ZFF
Name
Estimated Affinity
53U_H_2001
2D
53U_H_2001
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
Name (e.g. gly)
all
2ZFF
GLU1C
ALA1B
ASP1A
CYS1
GLY2
LEU3
ARG4
PRO5
LEU6
PHE7
GLU8
LYS9
LYS10
SER11
LEU12
GLU13
ASP14
LYS14A
THR14B
GLU14C
ARG14D
GLU14E
LEU14F
2ZFF
53U_H_2001
1 message

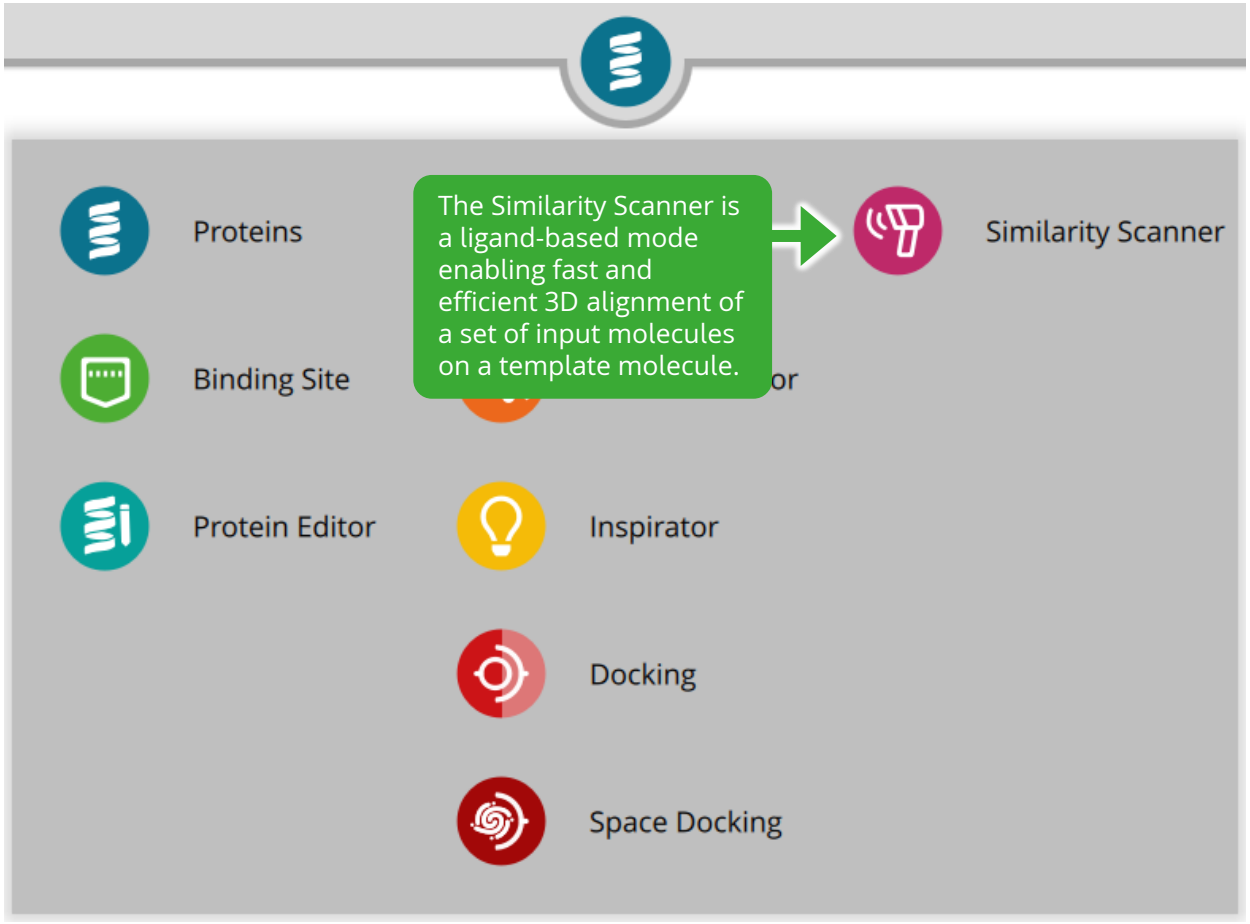

2ZFF
Data
Proteins
Filename
1
2ZFF
Tables:
• Collapse and re-open
• Drag rim to re-size
• Click entries to select
Ligand for 2ZFF
Name
Estimated Affi
pM
nM
µM
mM
53U_H_2001
2D
53U_H_2001
3D-viewer:
• Right-click to rotate
• Mouse-wheel to zoom
• Middle-click to shift
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
Name (e.g. gly)
all
2ZFF
GLU1C
ALA1B
ASP1A
CYS1
GLY2
LEU3
ARG4
PRO5
LEU6
PHE7
GLU8
LYS9
LYS10
SER11
LEU12
GLU13
ASP14
LYS14A
THR14B
GLU14C
ARG14D
GLU14E
LEU14F
2ZFF
53U_H_2001
1 message

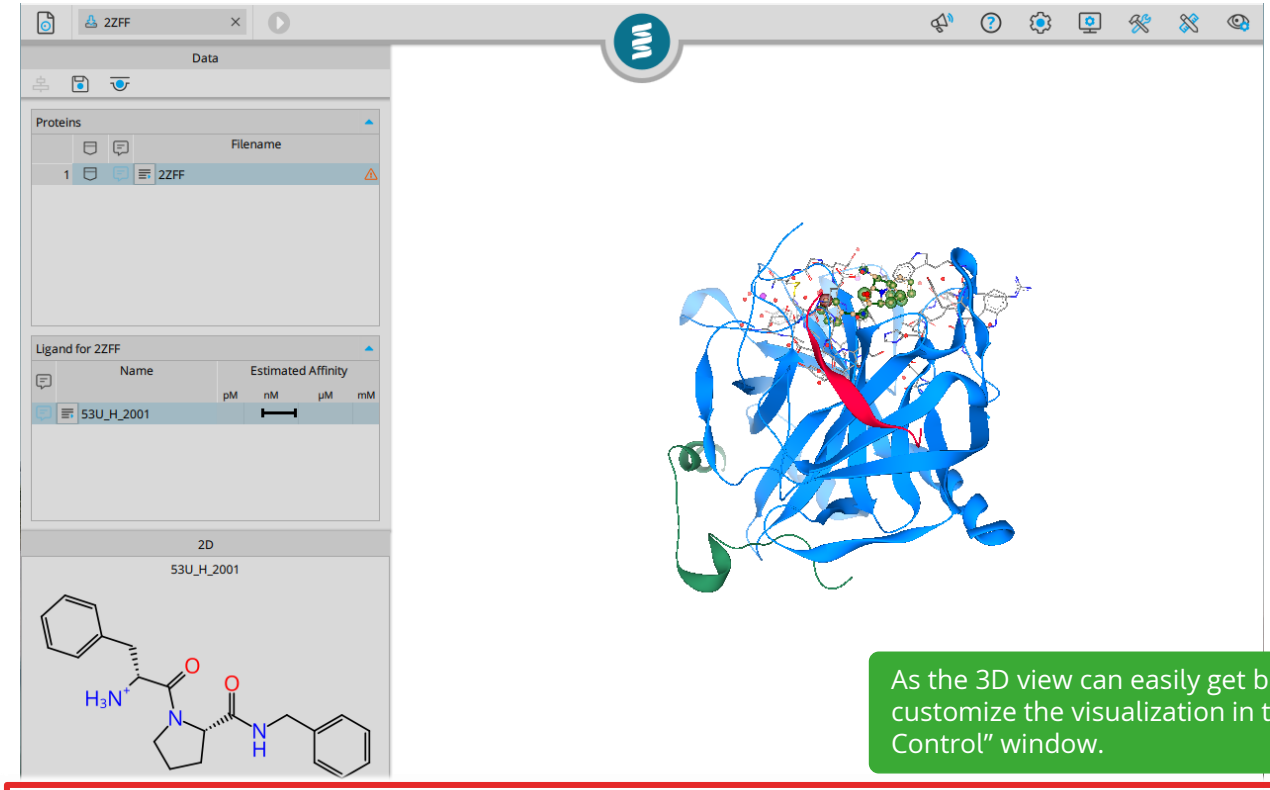

Change the table layout
Adjust label size
Adjust background color
Switch between dark and light theme
Switch to color blindness mode
If you want to customize the layout of SeeSAR, click on the “Appearance” button in the top right toolbar.
For this guide will use the light one, feel free to use whatever you prefer!
Data
Proteins
Filename
2ZFF
Ligand for 2ZFF
Name
Estimated Affinity
53U_H_2001
2D
Background
Change Color
Layout
Theme
Dark
Light
Label Size
Color Blindness
Green - Red
Blue - Red
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
1 message


2ZFF
Data
Proteins
Filename
1
Note that you are in **Protein mode**. The mode switch button indicates your current mode and also allows you to change modes. Hover over it to view your options.
Ligand for 2ZFF
Name
Estimated Affinity
pM
nM
µM
mM
53U_H_2001
2D
53U_H_2001
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
Name (e.g. gly)
all
2ZFF
GLU1C
ALA1B
ASP1A
CYS1
GLY2
LEU3
ARG4
PRO5
LEU6
PHE7
GLU8
LYS9
LYS10
SER11
LEU12
GLU13
ASP14
LYS14A
THR14B
GLU14C
ARG14D
GLU14E
LEU14F
2ZFF
53U_H_2001
1 message

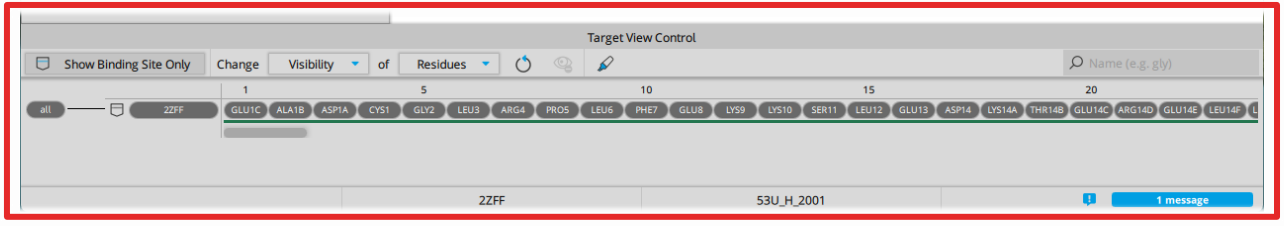

Proteins
In the Proteins mode you can load and superpose proteins.
Similarity Scanner
Binding Site
The Binding Site mode sets the reference pocket.
Protein Editor
The Protein Editor mode is for editing side chains, deleting waters or buffers, or search for similar binding sites.
Docking
Space Docking

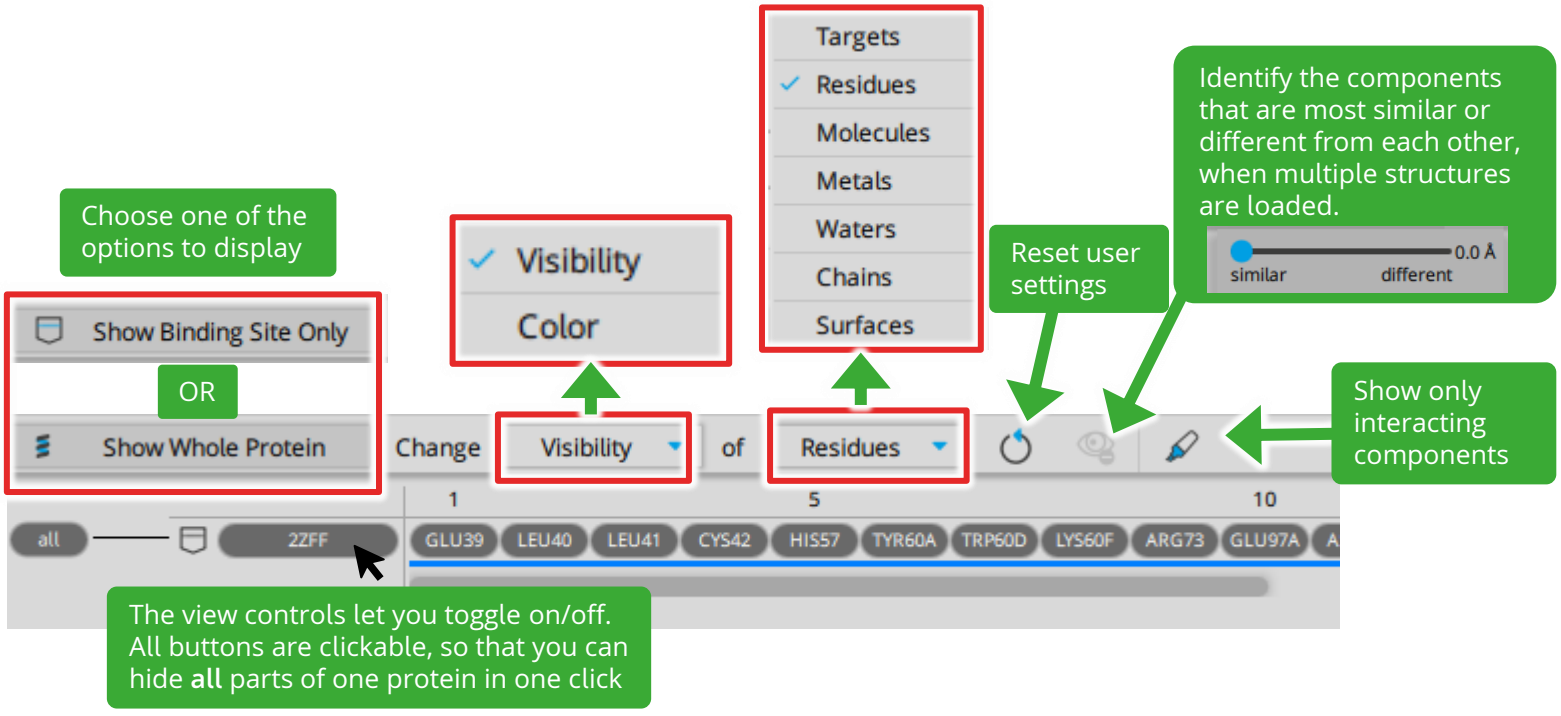

The Analyzer mode is for filtering molecule sets, hit triaging etc.
Analyzer
Similarity Scanner
The Molecule Editor mode is for designing new molecules in 3D.
Molecule Editor
In the Docking mode, you can generate poses for new molecules through molecular docking. It includes two sub-modes: dock in local machine and external server.
Inspirator
The Inspirator mode helps you to generate new ideas.
Docking
Hover over icon from the left for local machine.
From the right for the external server.
Space Docking
The Space Docking Mode was added in Version 14 of SeeSAR. It has its own dedicated section in this guide.
Jump to section


Proteins
Binding Site
Protein Editor
The Similarity Scanner is a ligand-based mode enabling fast and efficient 3D alignment of a set of input molecules on a template molecule.
Similarity Scanner
Inspirator
Docking
Space Docking

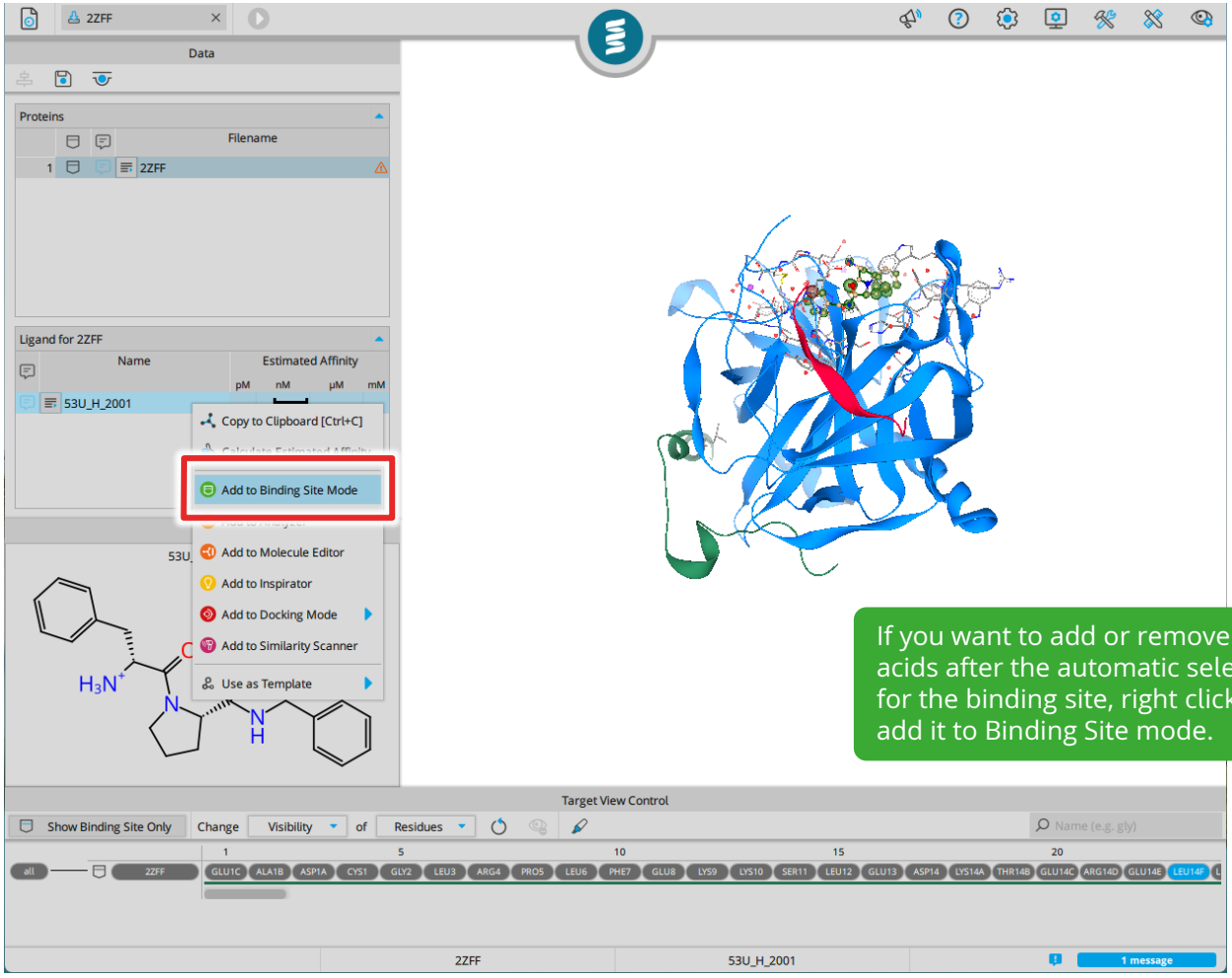


As the 3D view can easily get busy, let's customize the visualization in the "Target View Control" window.

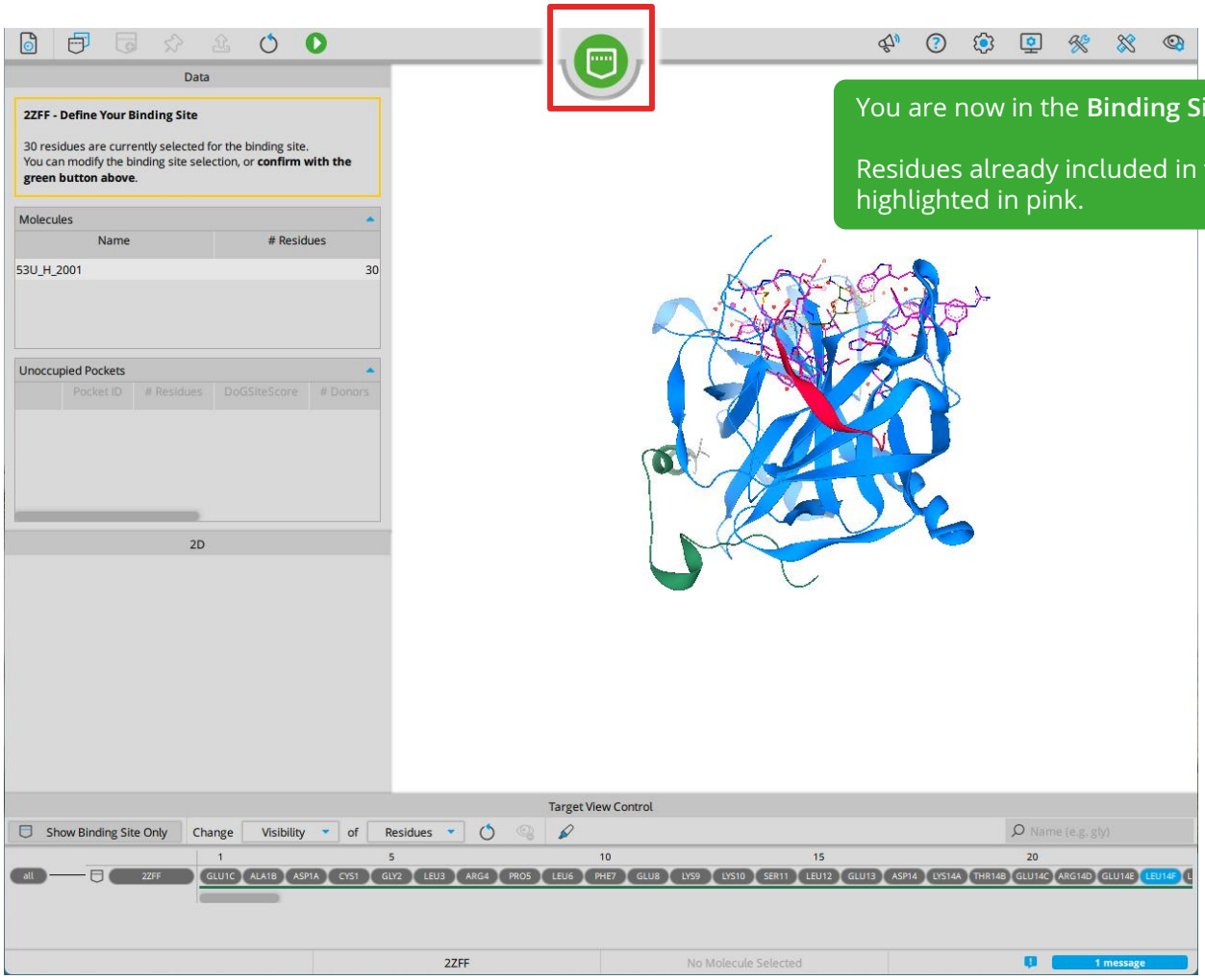


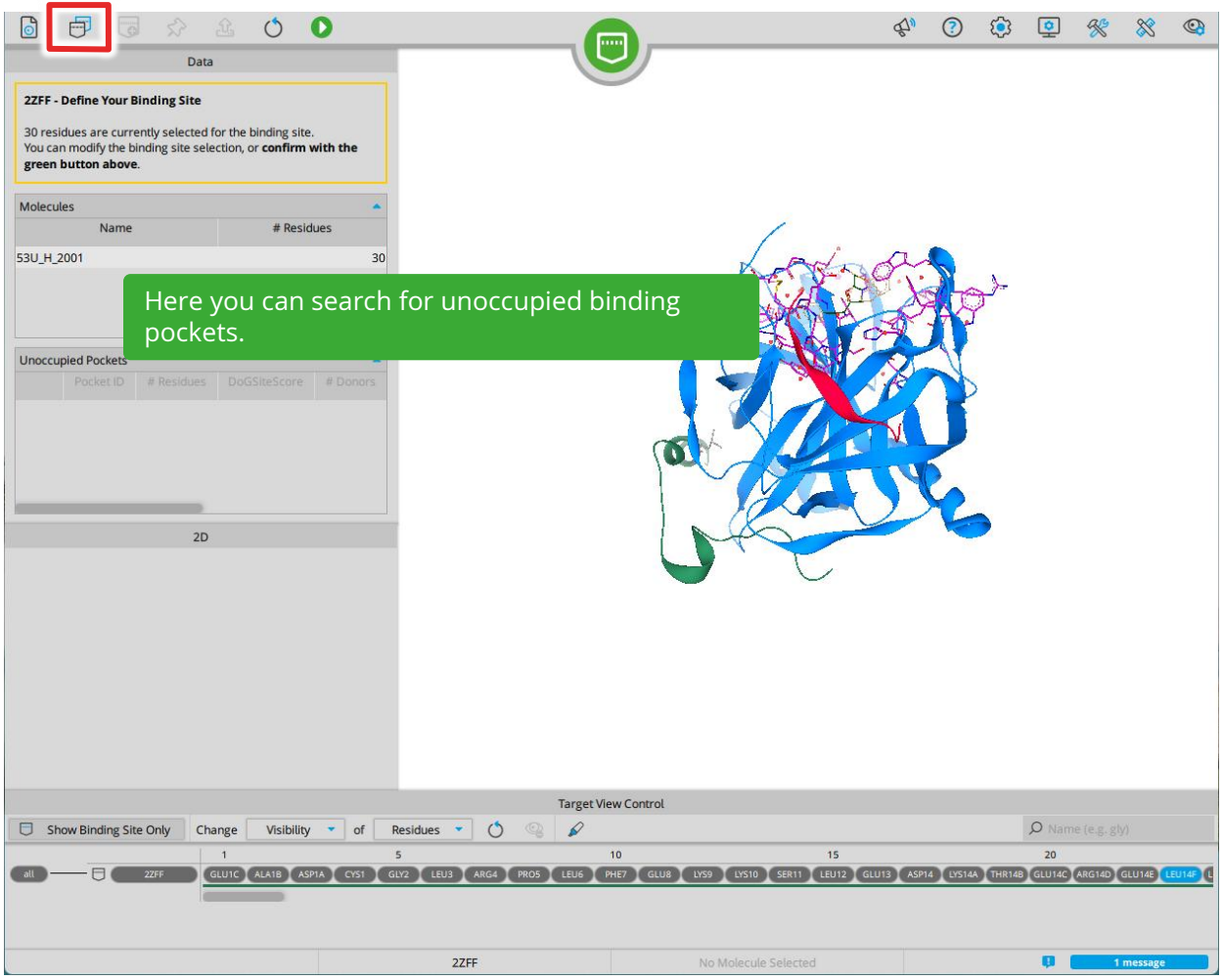


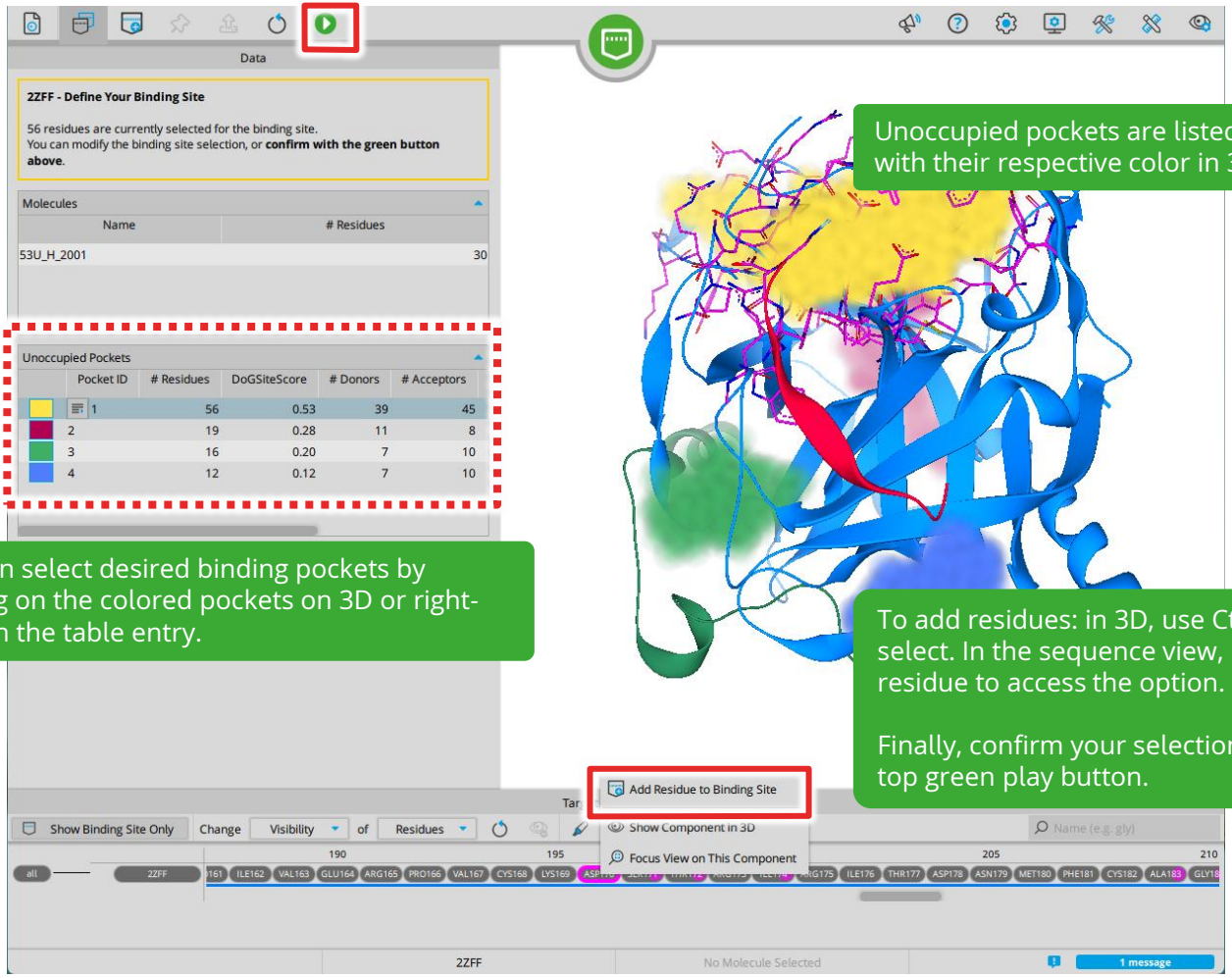
Example:
To visualize surface, select Change "Visibility" of "Surfaces" and toggle on the PDB code.
To adjust this surface visibility, set Change "Color" of "Surfaces" and right-click on PDB code to explore the options.



If you want to add or remove individual amino acids after the automatic selection of residues for the binding site, right click your ligand and add it to Binding Site mode.


Data
2ZFF - Define Your Binding Site
30 residues are currently selected for the binding site.
You can modify the binding site selection, or confirm with the green button above.
Molecules
Name
Residues
53U_H_2001
30
Unoccupied Pockets
Pocket ID
Residues
DoGSiteScore
Donors
2D
You are now in the Binding Site mode.
Residues already included in the binding site are highlighted in pink.
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
Name (e.g. gly)
all
2ZFF
GLU1C
ALA1B
ASP1A
CYS1
GLY2
LEU3
ARG4
PRO5
LEU6
PHE7
GLU8
LYS9
LYS10
SER11
LEU12
GLU13
ASP14
LYS14A
THR14B
GLU14C
ARG14D
GLU14E
LEU14F
2ZFF
No Molecule Selected
1 message


Data
2ZFF - Define Your Binding Site
30 residues are currently selected for the binding site.
You can modify the binding site selection, or confirm with the green button above.
Molecules
Name
Residues
53U_H_2001
30
Unoccupied Pockets
Pocket ID
Residues
DoGSiteScore
Donors
2D
Here you can search for unoccupied binding pockets.
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
Name (e.g. gly)
2ZFF
No Molecule Selected
1 message

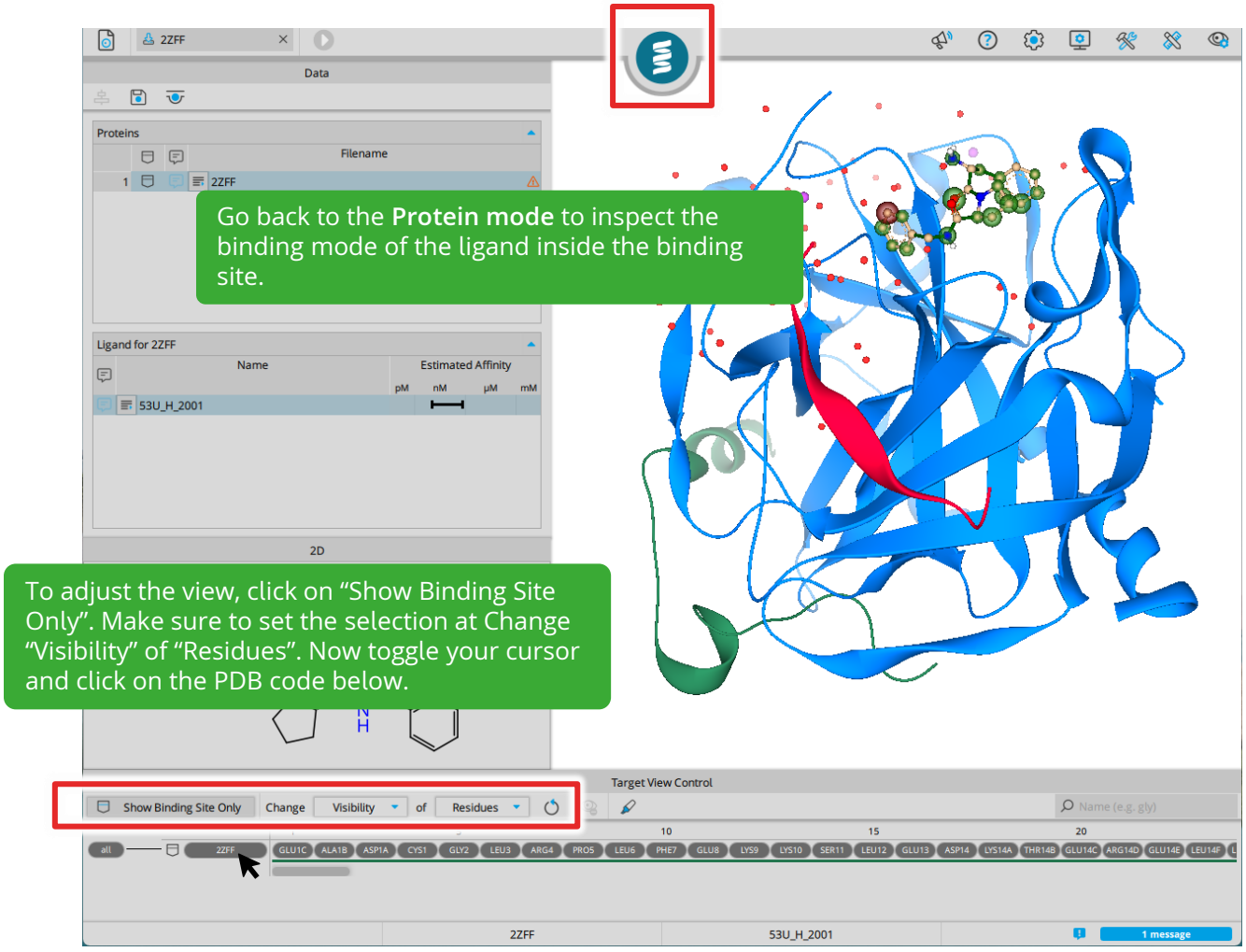


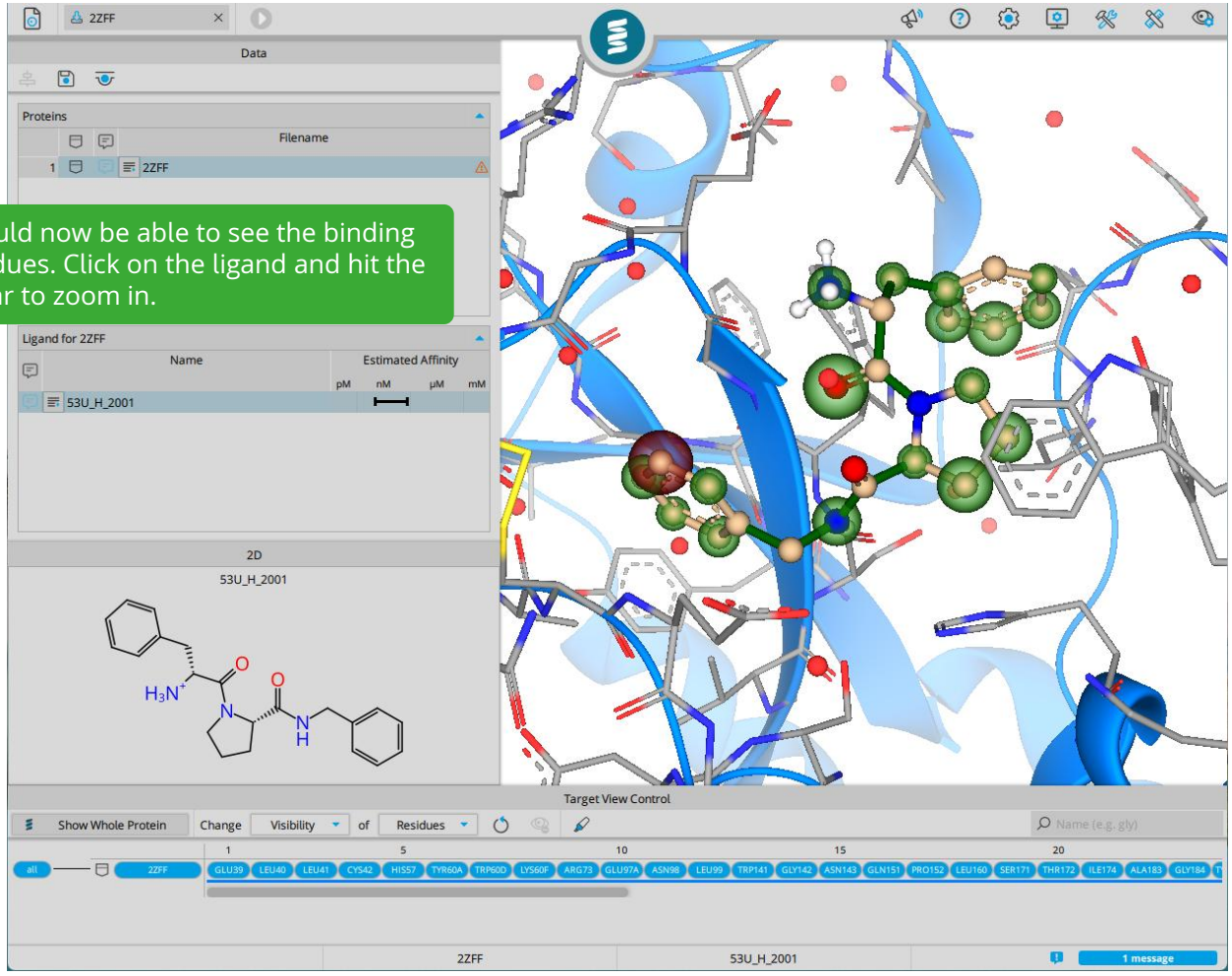
Unoccupied pockets are listed and presented with their respective color in 3D.

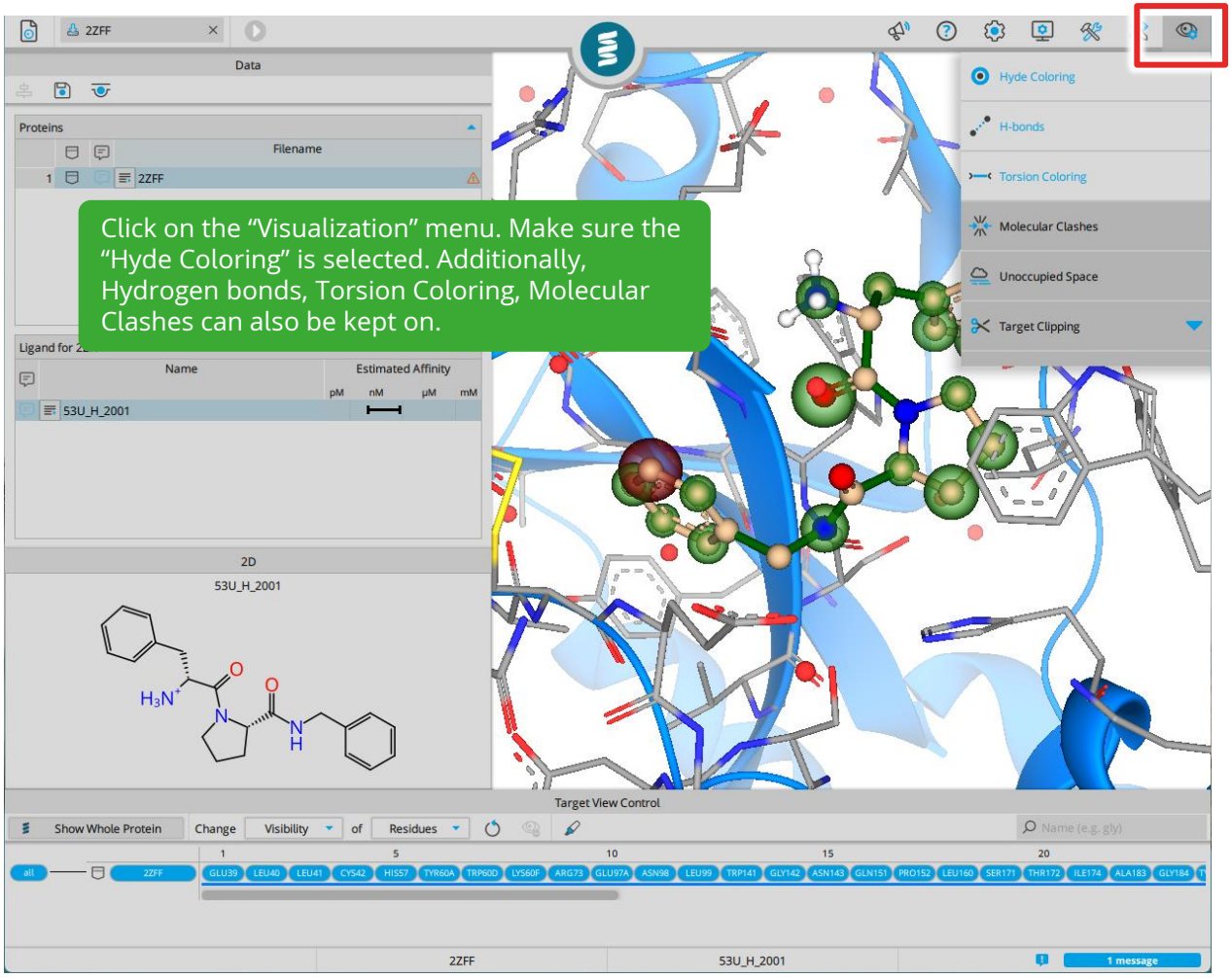
You can select desired binding pockets by clicking on the colored pockets on 3D or right-click on the table entry.

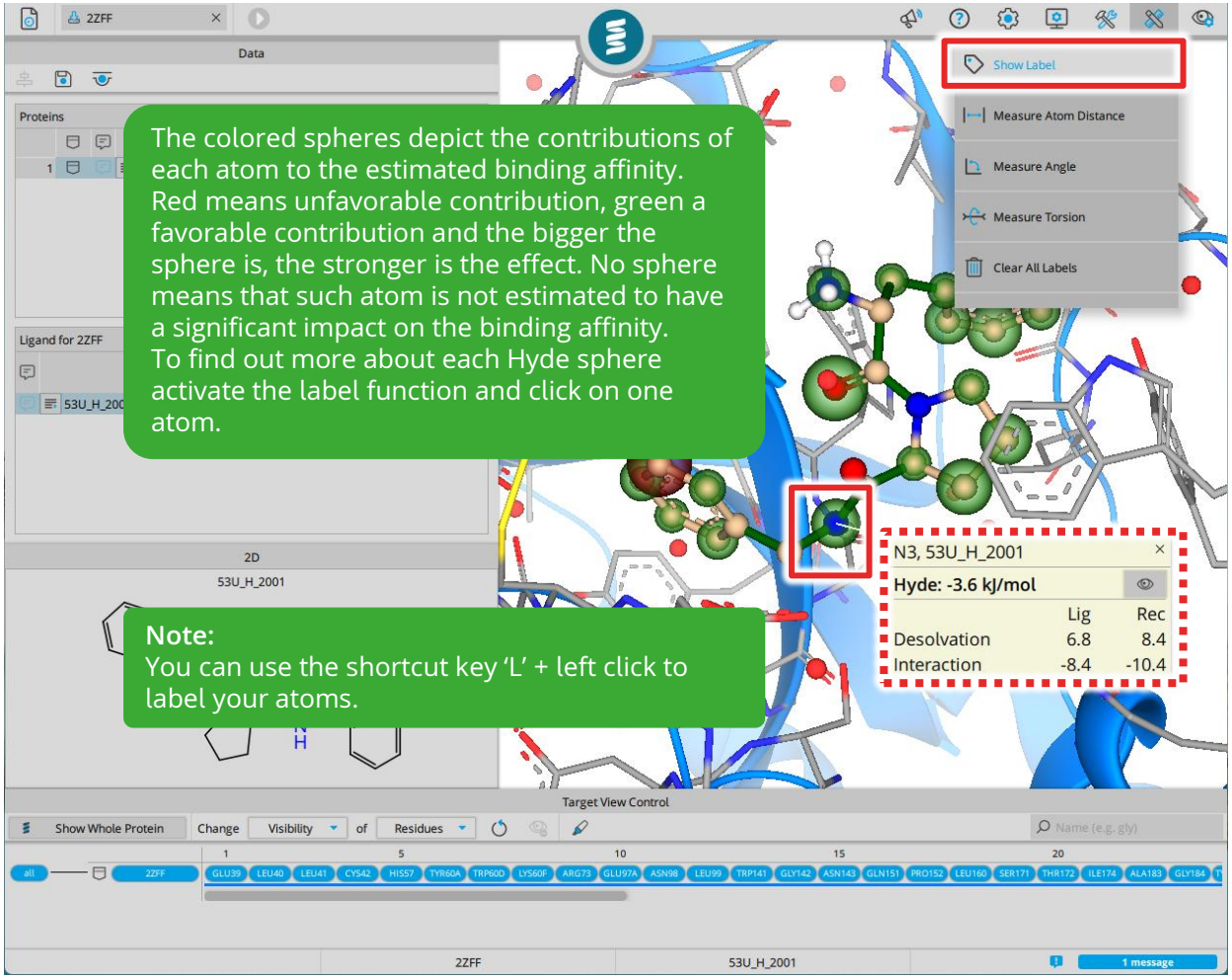
To add residues: in 3D, use Ctrl + left click to select. In the sequence view, right-click on a residue to access the option.

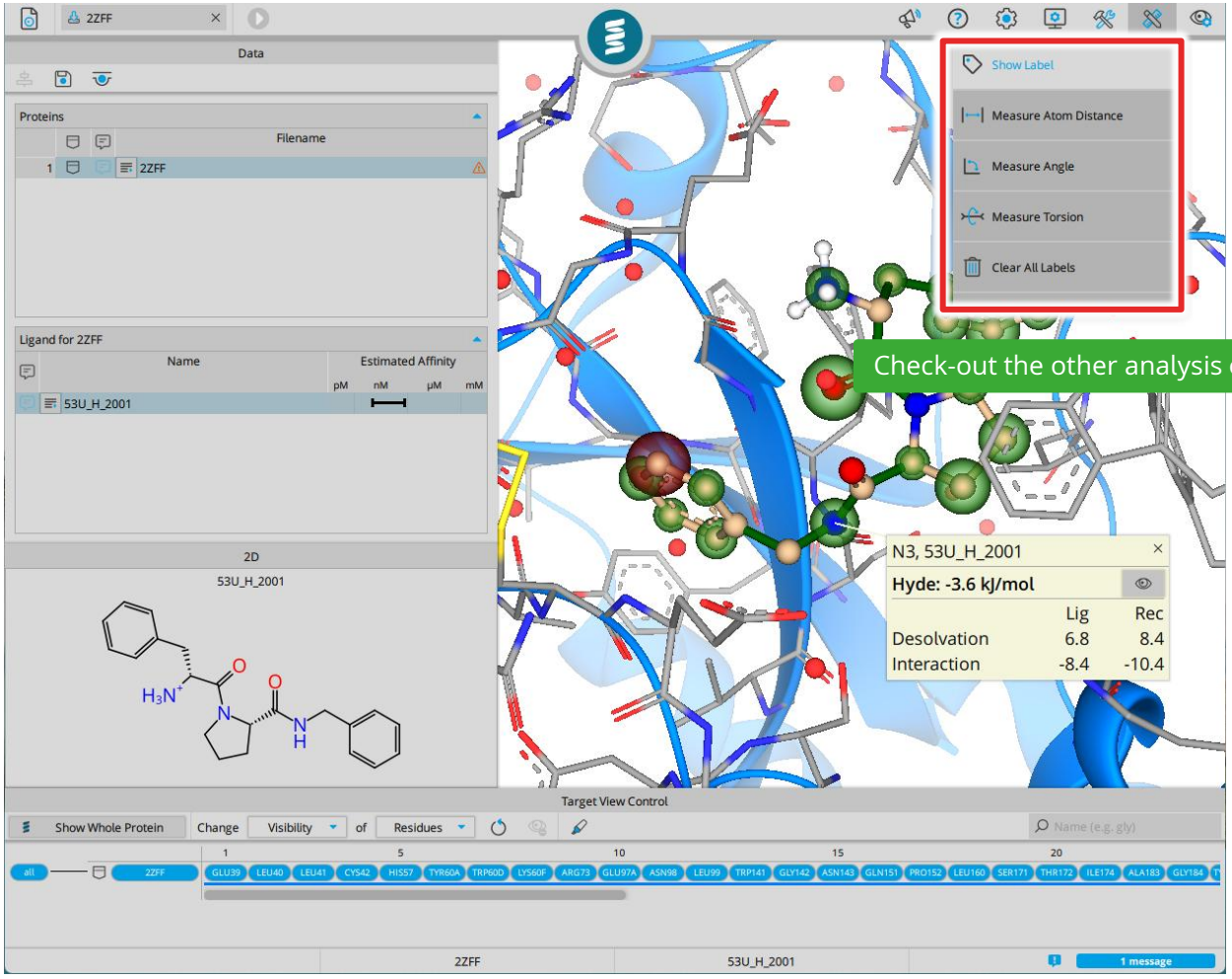
Finally, confirm your selection by clicking on the top green play button.

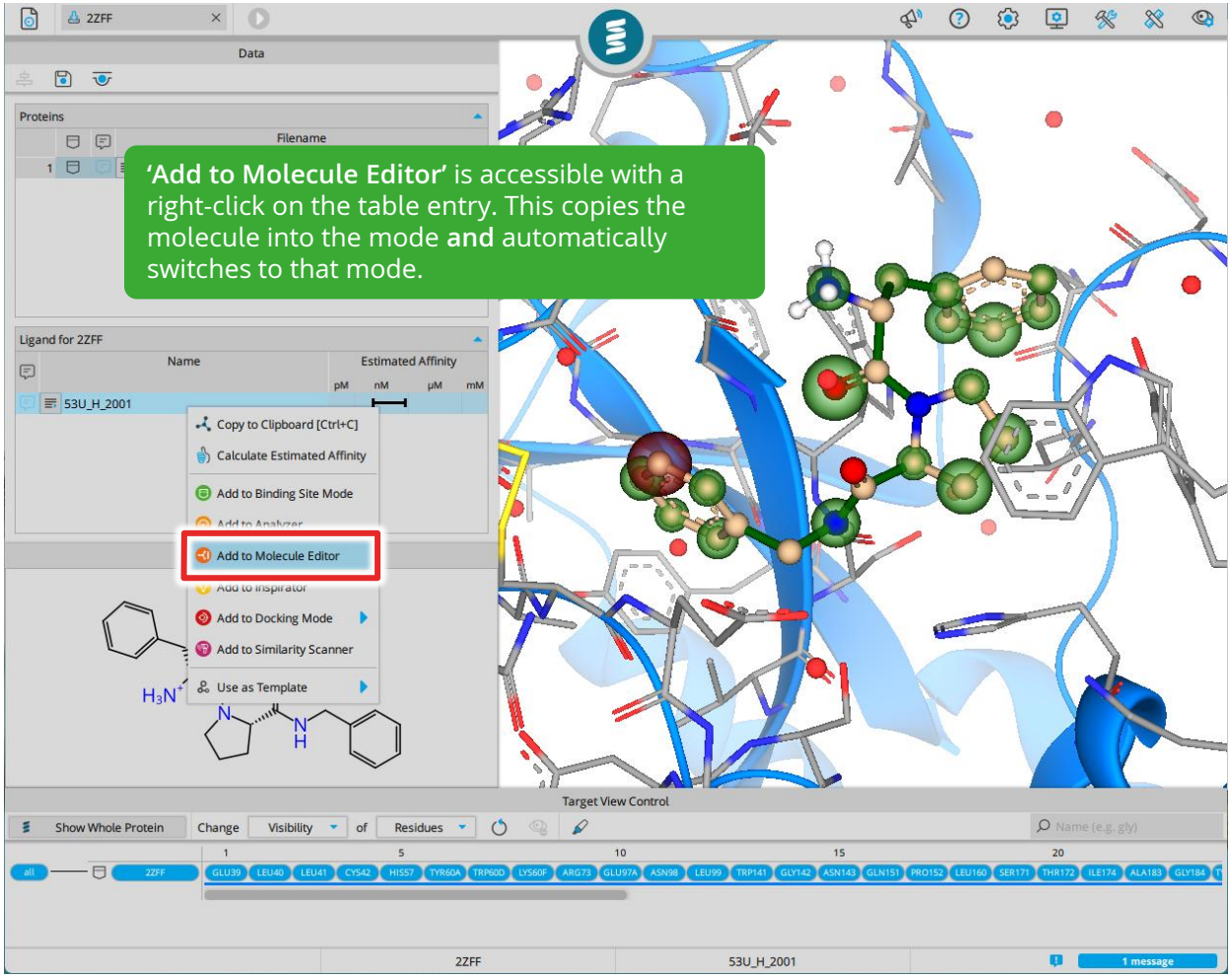

2ZFF
Data
Proteins
Filename
1
2ZFF
Go back to the **Protein mode** to inspect the binding mode of the ligand inside the binding site.
Ligand for 2ZFF
Name
Estimated Affinity
pM
nM
µM
mM
53U_H_2001
2D
To adjust the view, click on “Show Binding Site Only”. Make sure to set the selection at Change “Visibility” of “Residues”. Now toggle your cursor and click on the PDB code below.
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
Name (e.g. gly)
10
15
20
all
2ZFF
GLU1C
ALA1B
ASP1A
CYS1
GLY2
LEU3
ARG4
PRO5
LEU6
PHE7
GLU8
LYS9
LYS10
SER11
LEU12
GLU13
ASP14
LYS14A
THR14B
GLU14C
ARG14D
GLU14E
LEU14F
2ZFF
53U_H_2001
1 message


2ZFF
Data
Proteins
Filename
1
2ZFF
You should now be able to see the binding site residues. Click on the ligand and hit the space bar to zoom in.
Ligand for 2ZFF
Name
Estimated Affinity
pM
nM
µM
mM
53U_H_2001
2D
53U_H_2001
Target View Control
Show Whole Protein
Change
Visibility
of
Residues
Name (e.g. gly)
all
2ZFF
GLU39
LEU40
LEU41
CYS42
HIS57
TYR60A
TRP60D
LYS60F
ARG73
GLU97A
ASN98
LEU99
TRP141
GLY142
ASN143
GLN151
PRO152
LEU160
SER171
THR172
ILE174
ALA183
GLY184
2ZFF
53U_H_2001
1 message


2ZFF
Data
Proteins
Filename
1
2ZFF
Click on the “Visualization” menu. Make sure the “Hyde Coloring” is selected. Additionally, Hydrogen bonds, Torsion Coloring, Molecular Clashes can also be kept on.
Name
Estimated Affinity
pM
nM
µM
mM
53U_H_2001
2D
53U_H_2001
Hyde Coloring
H-bonds
Torsion Coloring
Molecular Clashes
Unoccupied Space
Target Clipping
Target View Control
Show Whole Protein
Change
Visibility
of
Residues
Name (e.g. gly)
all
2ZFF
GLU39
LEU40
LEU41
CYS42
HIS57
TYR60A
TRP60D
LYS60F
ARG73
GLU97A
ASN98
LEU99
TRP141
GLY142
ASN143
GLN151
PRO152
LEU160
SER171
THR172
ILE174
ALA183
GLY184
2ZFF
53U_H_2001
1 message


2ZFF
Data
Proteins
Ligand for 2ZFF
2D
53U_H_2001
Show Label
Measure Atom Distance
Measure Angle
Measure Torsion
Clear All Labels
N3, 53U_H_2001
Hyde: -3.6 kJ/mol
Lig Rec
Desolvation 6.8 8.4
Interaction -8.4 -10.4
The colored spheres depict the contributions of each atom to the estimated binding affinity. Red means unfavorable contribution, green a favorable contribution and the bigger the sphere is, the stronger is the effect. No sphere means that such atom is not estimated to have a significant impact on the binding affinity.
To find out more about each Hyde sphere activate the label function and click on one atom.
Note:
You can use the shortcut key 'L' + left click to label your atoms.
Target View Control
Show Whole Protein
Change
Visibility
of
Residues
2ZFF
53U_H_2001
1 message


2ZFF
Data
Proteins
Filename
1
2ZFF
Ligand for 2ZFF
Name
Estimated Affinity
pM
nM
µM
mM
53U_H_2001
2D
53U_H_2001
Show Label
Measure Atom Distance
Measure Angle
Measure Torsion
Clear All Labels
Check-out the other analysis options!
N3, 53U_H_2001
Hyde: -3.6 kJ/mol
Lig
Rec
Desolvation
6.8
8.4
Interaction
-8.4
-10.4
Target View Control
Show Whole Protein
Change
Visibility
of
Residues
Name (e.g. gly)
all
2ZFF
GLU39
LEU40
LEU41
CYS42
HIS57
TYR60A
TRP60D
LYS60F
ARG73
GLU97A
ASN98
LEU99
TRP141
GLY142
ASN143
GLN151
PRO152
LEU160
SER171
THR172
ILE174
ALA183
GLY184
2ZFF
53U_H_2001
1 message


2ZFF
Data
Proteins
Filename
1
'Add to Molecule Editor' is accessible with a right-click on the table entry. This copies the molecule into the mode and automatically switches to that mode.
Ligand for 2ZFF
Name
Estimated Affinity
pM
nM
µM
mM
53U_H_2001
Copy to Clipboard [Ctrl+C]
Calculate Estimated Affinity
Add to Binding Site Mode
Add to Molecule Editor
Add to Docking Mode
Add to Similarity Scanner
Use as Template
Target View Control
Show Whole Protein
Change
Visibility
of
Residues
Name (e.g. gly)
all
2ZFF
GLU39
LEU40
LEU41
CYS42
HIS57
TYR60A
TRP60D
LYS60F
ARG73
GLU97A
ASN98
LEU99
TRP141
GLY142
ASN143
GLN151
PRO152
LEU160
SER171
THR172
ILE174
ALA183
GLY184
2ZFF
53U_H_2001
1 message

The editor-menu will appear on the top left.
There you can:

Add atoms or rings

Change charge

Adjust torsion

Remove atoms

Store the new molecule to the table after a template-based docking

Create a new molecule

Change atom type

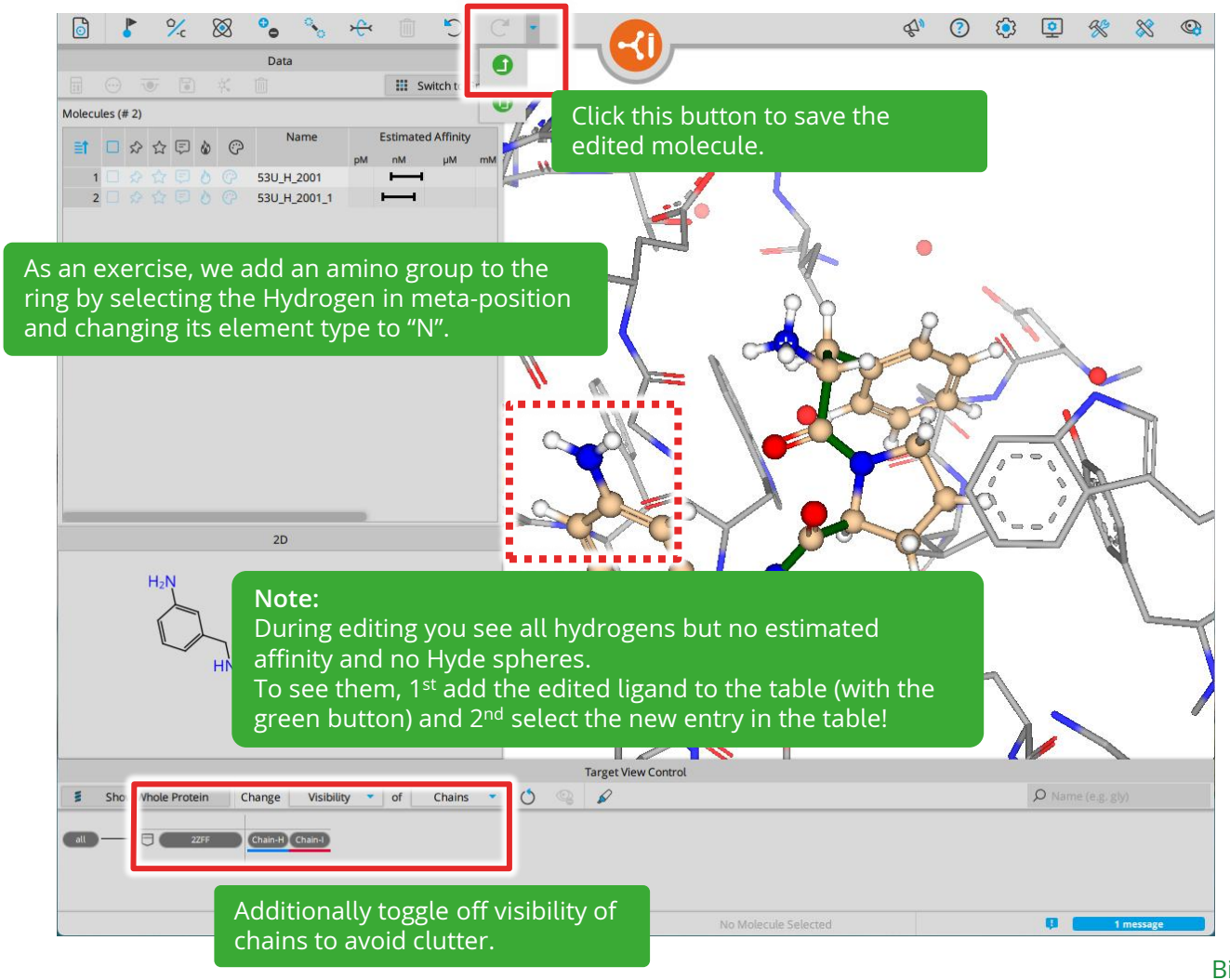
Change bond type

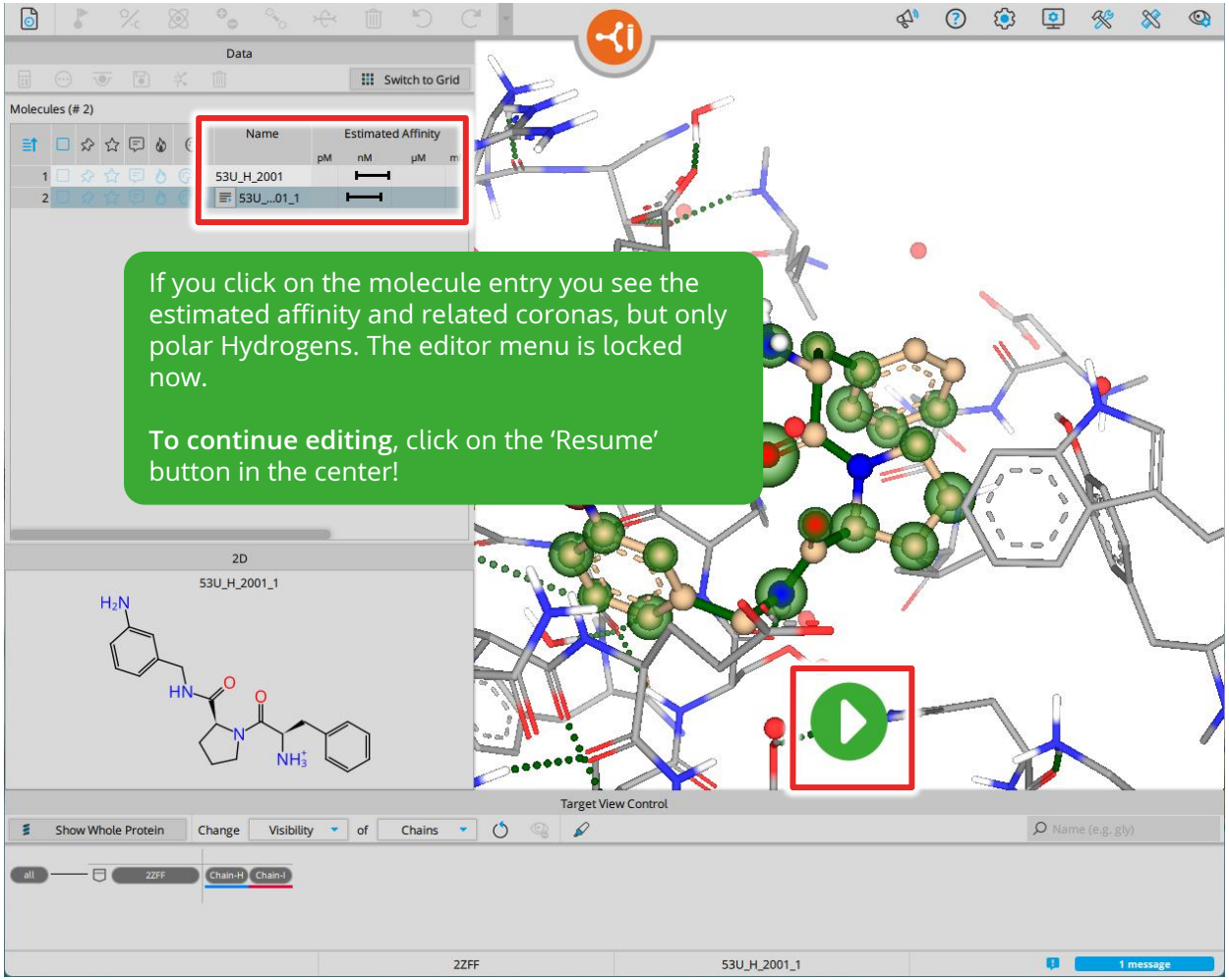
Undo/redo

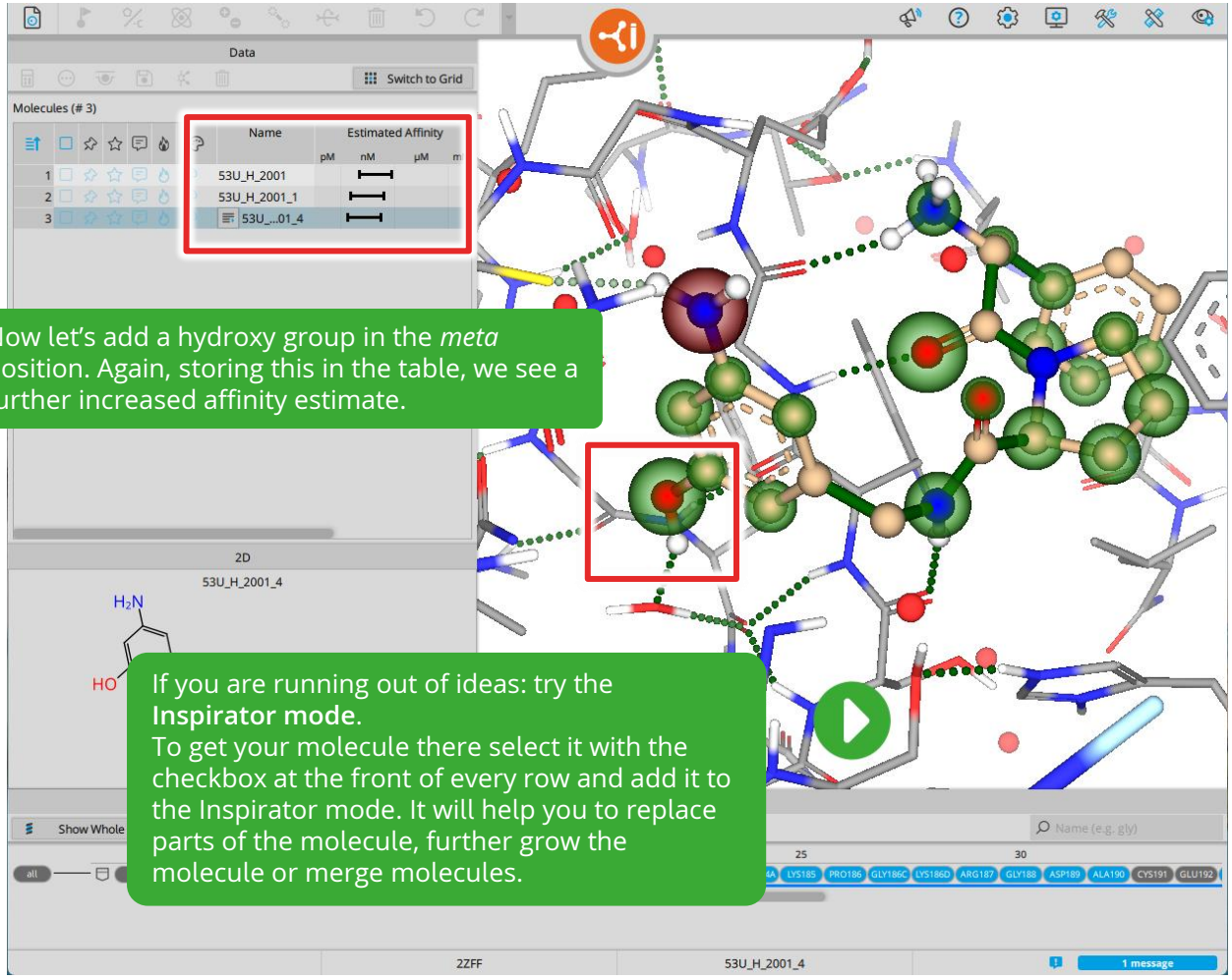
Store the current molecule to the table

To edit a molecule ALWAYS:
1. **select** (atoms or bonds)
2. **modify** (using the function of choice from above)

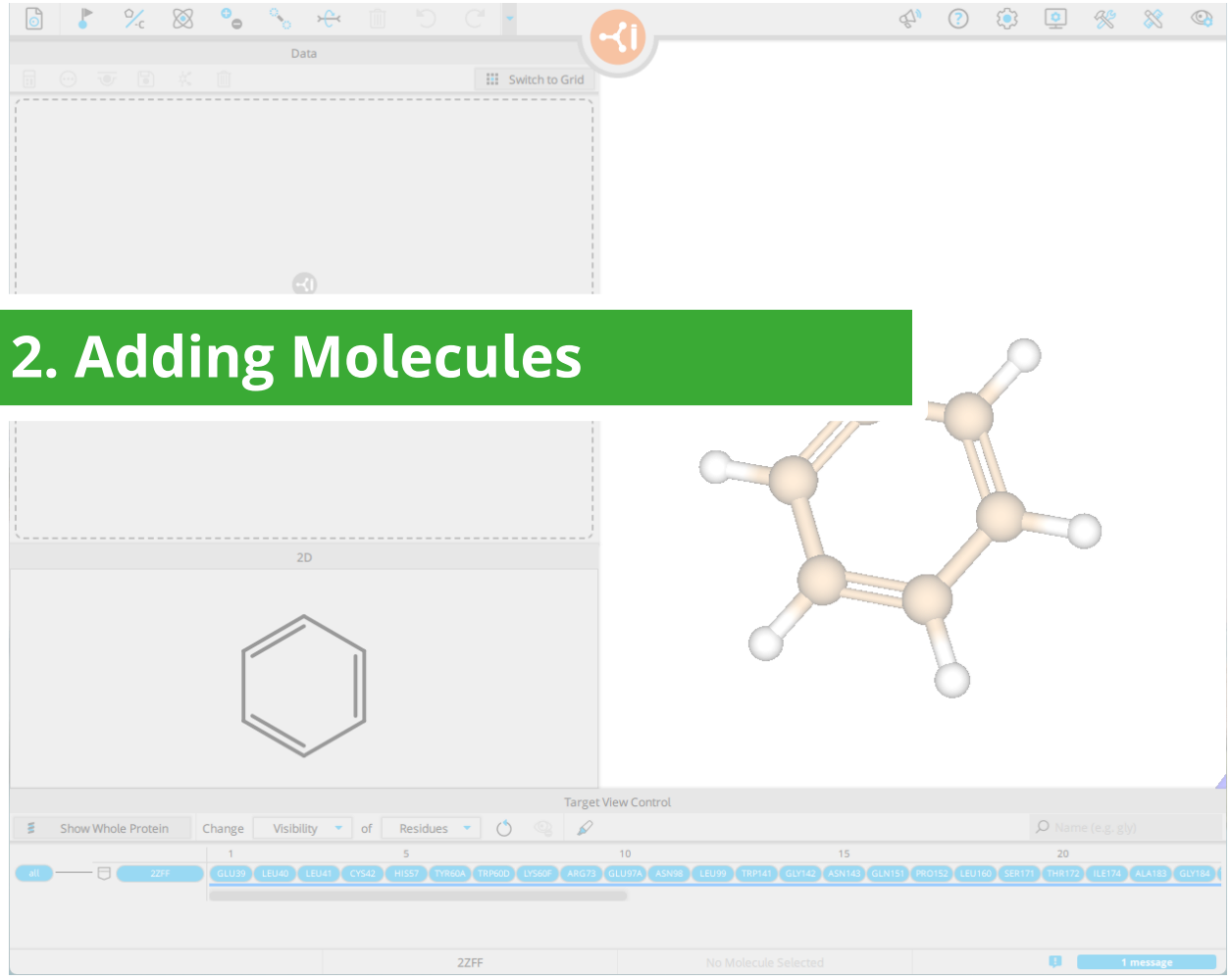
Note that many editor functions have shortcut-keys.
E.g. select a bond and type 1, 2 or, 3 on the keyboard, or select an atom and type the element (C, N, O, ...).

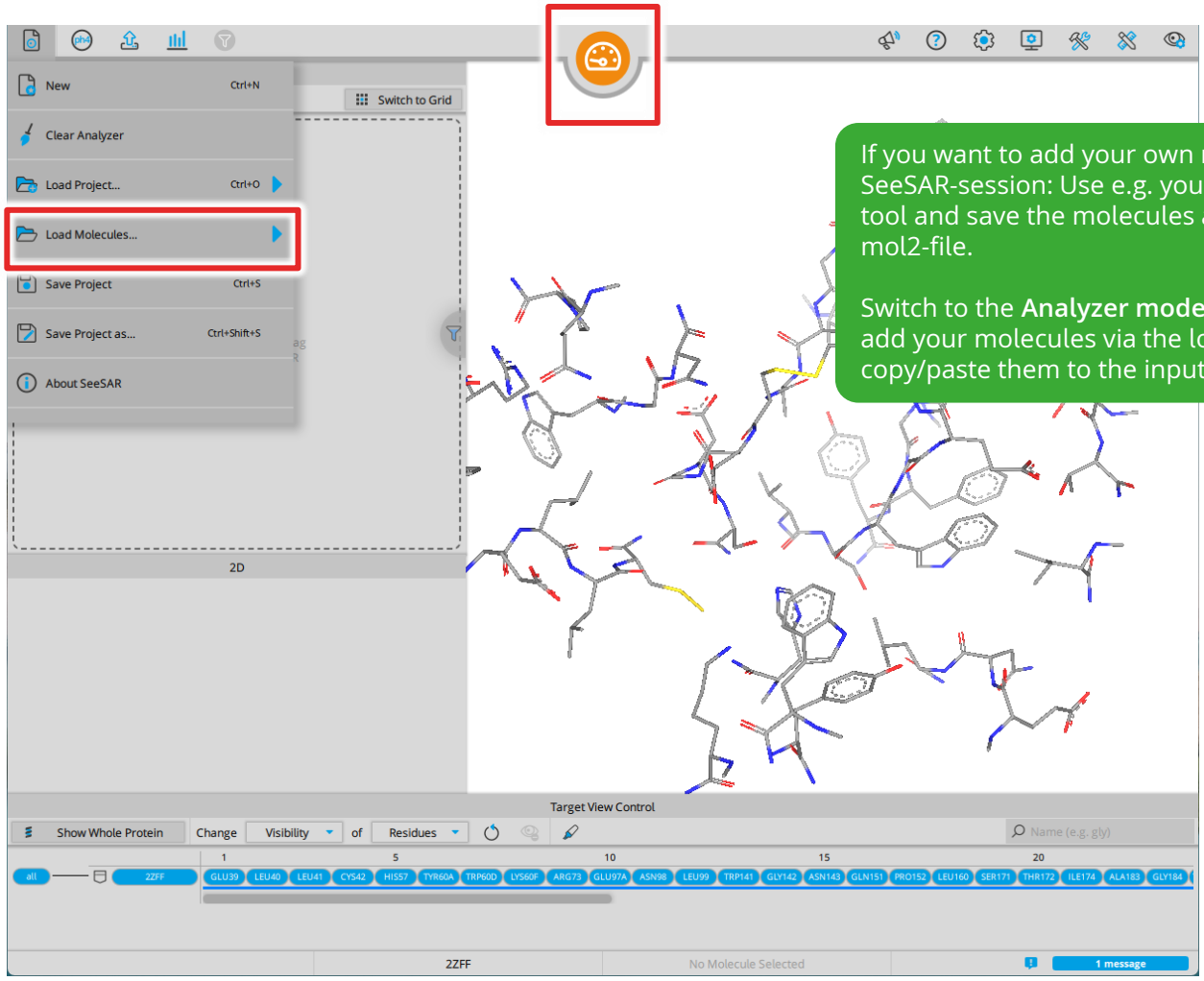

Click this button to save the edited molecule.
As an exercise, we add an amino group to the ring by selecting the Hydrogen in meta-position and changing its element type to “N”.
Note:
During editing you see all hydrogens but no estimated affinity and no Hyde spheres.
To see them, 1st add the edited ligand to the table (with the green button) and 2nd select the new entry in the table!
Additionally toggle off visibility of chains to avoid clutter.
Data
Molecules (# 2)
Name
Estimated Affinity
53U_H_2001
53U_H_2001_1
2D
Target View Control
Whole Protein
Change
Visibility
of
Chains
2ZFF
Chain-H
Chain-I
No Molecule Selected
1 message


Data
Switch to Grid
Molecules (# 2)
Name
Estimated Affinity
pM
nM
µM
53U_H_2001
53U_...01_1
If you click on the molecule entry you see the estimated affinity and related coronas, but only polar Hydrogens. The editor menu is locked now.
To continue editing, click on the 'Resume' button in the center!
2D
53U_H_2001_1
Target View Control
Show Whole Protein
Change
Visibility
of
Chains
Name (e.g. gly)
all
2ZFF
Chain-H
Chain-I
2ZFF
53U_H_2001_1
1 message


Data
Switch to Grid
Molecules (# 3)
Name
Estimated Affinity
pM
nM
µM
m
1
53U_H_2001
2
53U_H_2001_1
3
53U_...01_4
Now let's add a hydroxy group in the *meta* position. Again, storing this in the table, we see a further increased affinity estimate.
2D
53U_H_2001_4
H_2N
HO
If you are running out of ideas: try the **Inspirator mode**.
To get your molecule there select it with the checkbox at the front of every row and add it to the Inspirator mode. It will help you to replace parts of the molecule, further grow the molecule or merge molecules.
Show Whole
Name (e.g. gly)
25
30
all
LYS185
PRO186
GLY186C
LYS186D
ARG187
GLY188
ASP189
ALA190
CYS191
GLU192
2ZFF
53U_H_2001_4
1 message

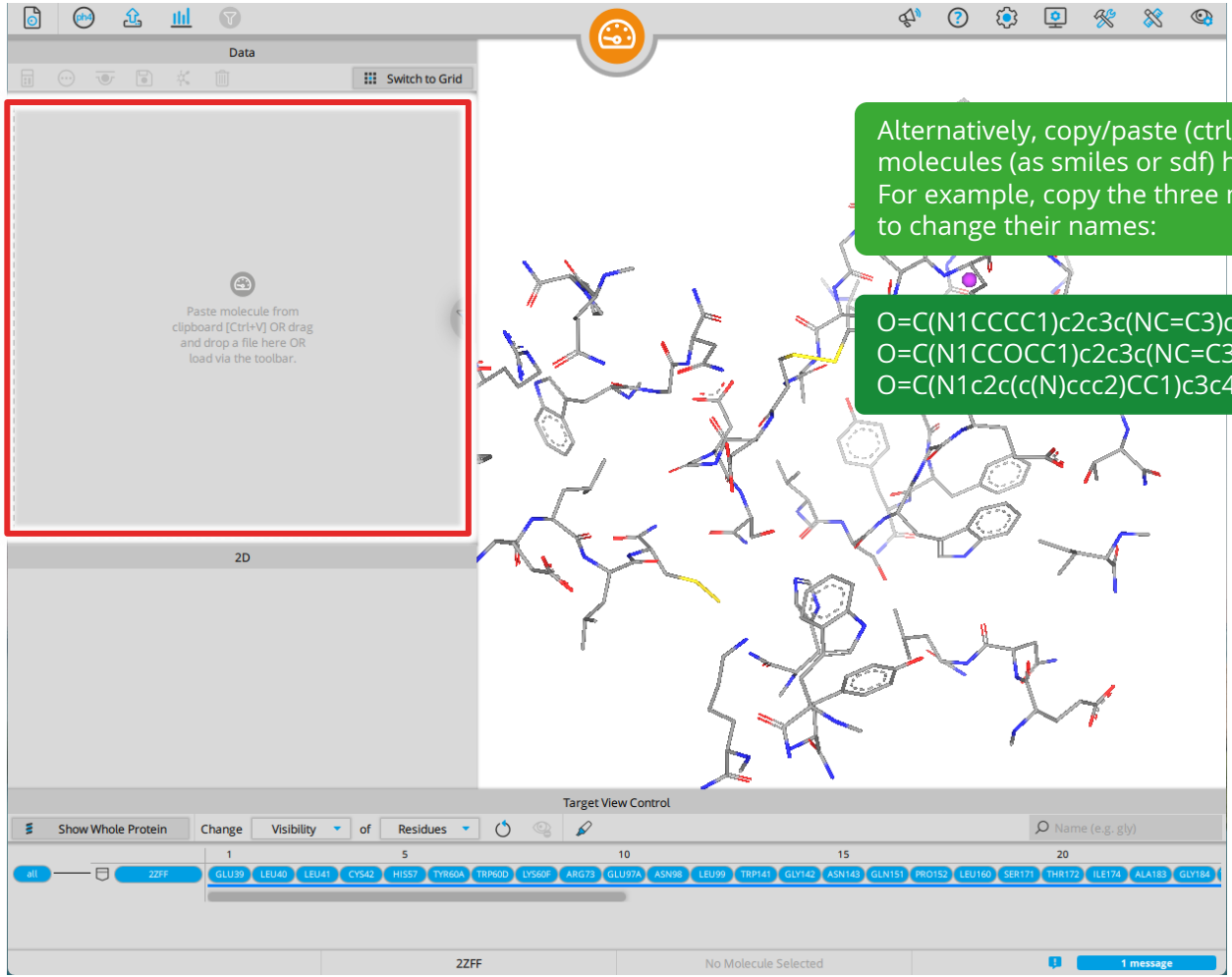
2. Adding Molecules

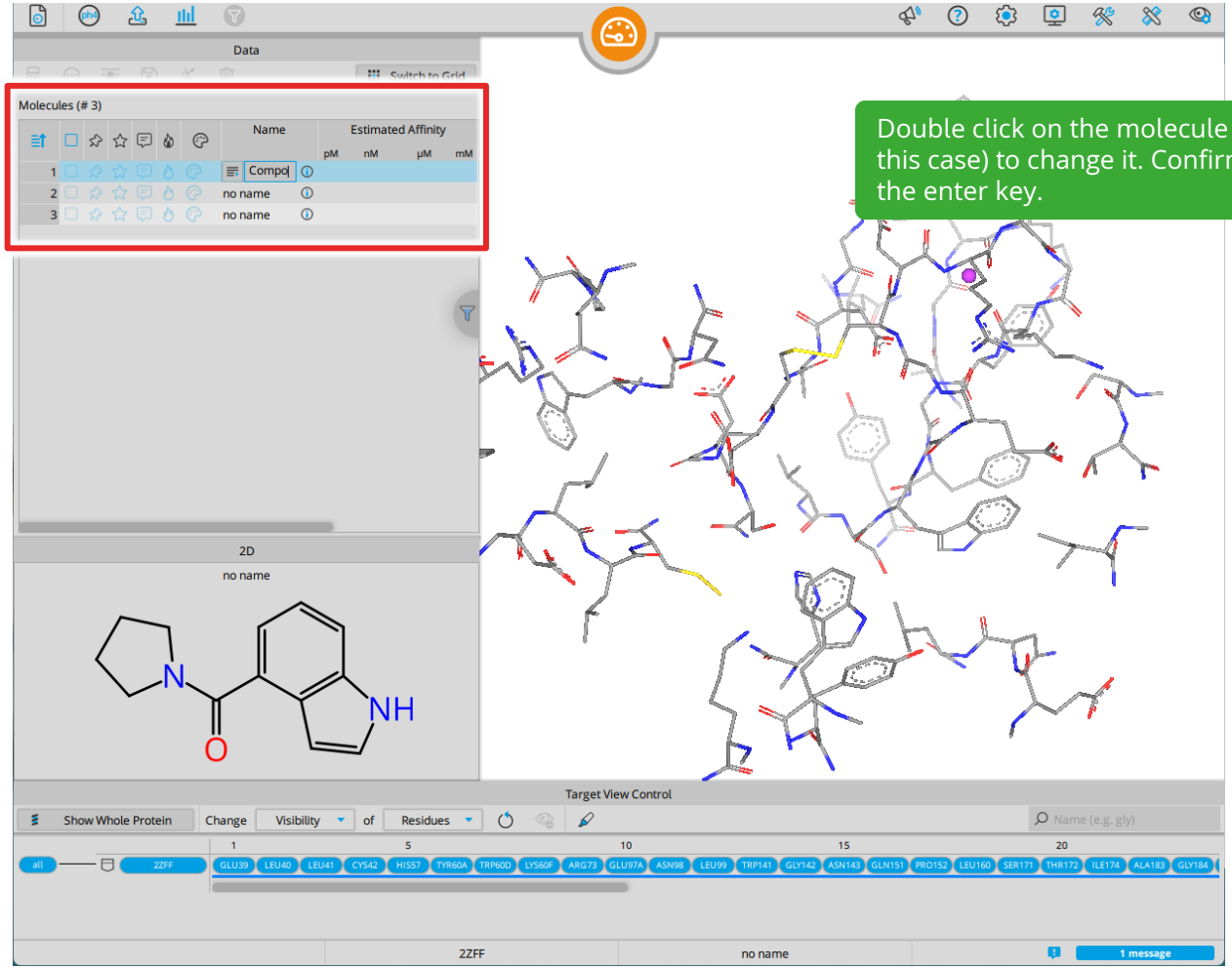




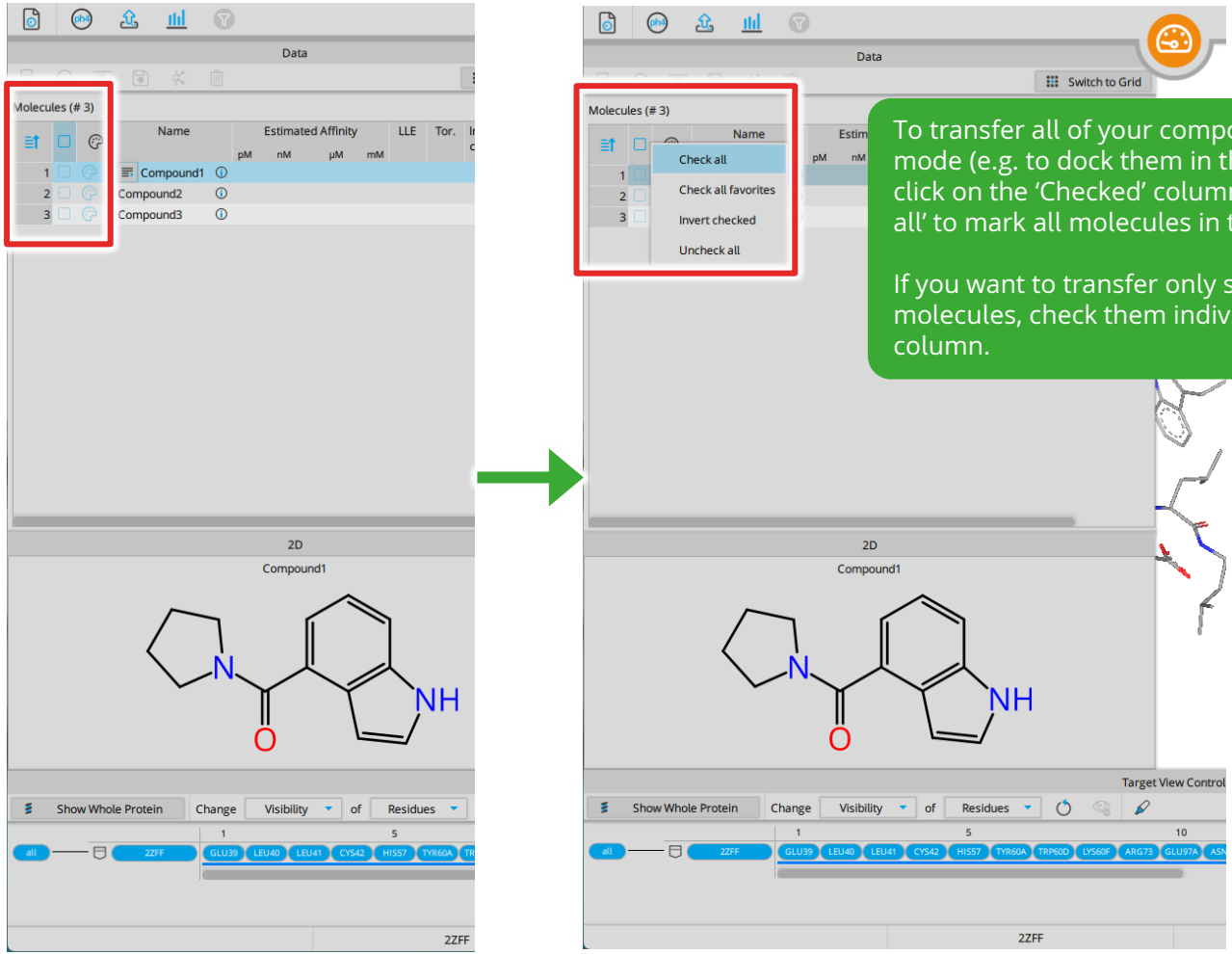
If you want to add your own molecules to a SeeSAR-session: Use e.g. your favorite drawing tool and save the molecules as sdf-, smiles-, or mol2-file.

Switch to the **Analyzer mode** in SeeSAR and add your molecules via the load button or copy/paste them to the input library field.


Data
Switch to Grid
Paste molecule from clipboard [Ctrl+V] OR drag and drop a file here OR load via the toolbar.
2D
Alternatively, copy/paste (ctrl + c/ctrl + v) your molecules (as smiles or sdf) here.
For example, copy the three molecules below, to change their names:
O=C(N1CCCC1)c2c3c(NC=C3)ccc2
O=C(N1CCOCC1)c2c3c(NC=C3)ccc2
O=C(N1c2c(c(N)ccc2)CC1)c3c4c(NC=C4)ccc3
Target View Control
Show Whole Protein
Change
Visibility
of
Residues
Name (e.g. gly)
all
2ZFF
GLU39
LEU40
LEU41
CYS42
HIS57
TYR60A
TRP60D
LYS60F
ARG73
GLU97A
ASN98
LEU99
TRP141
GLY142
ASN143
GLN151
PRO152
LEU160
SER171
THR172
ILE174
ALA183
GLY184
2ZFF
No Molecule Selected
1 message

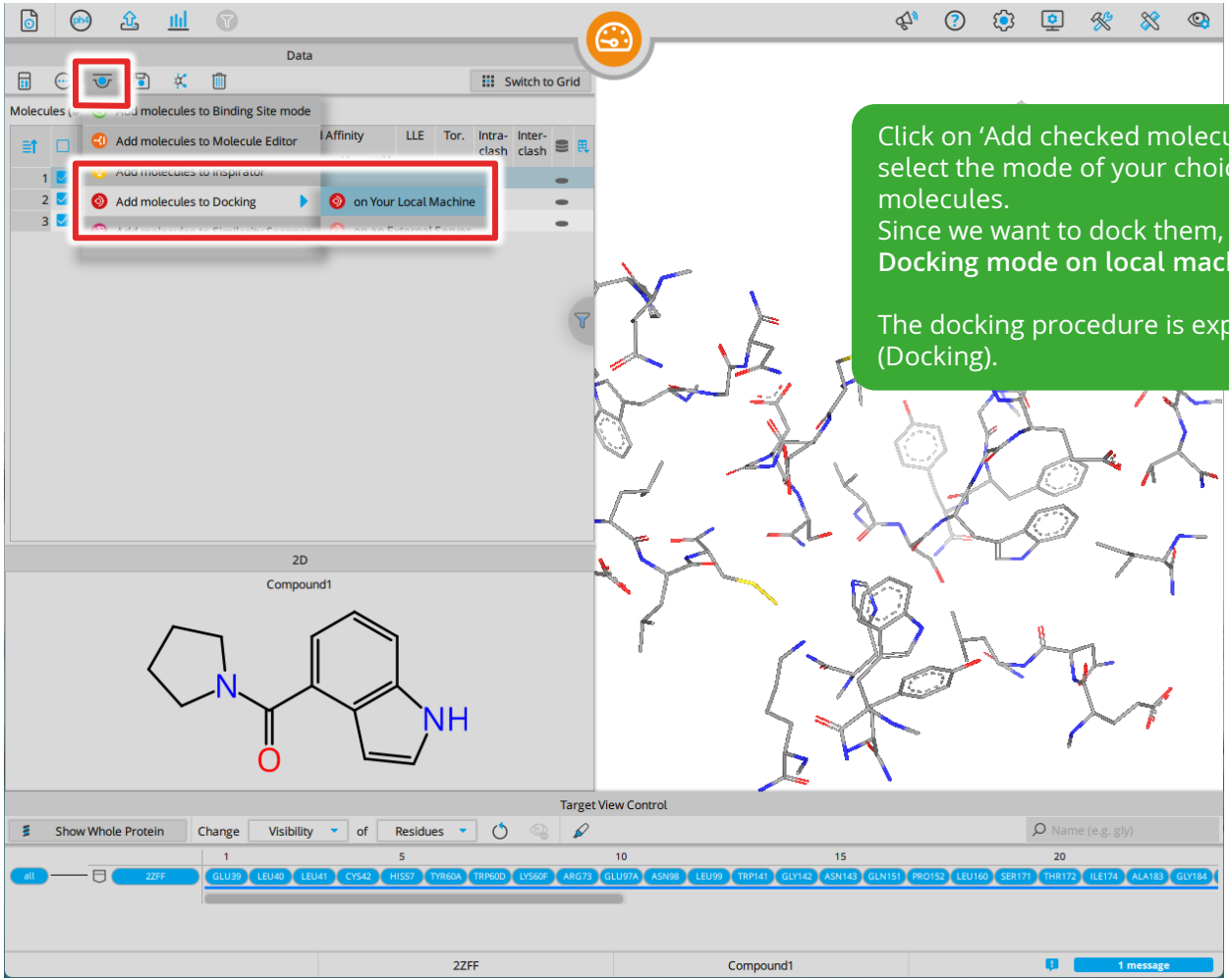


Double click on the molecule name (‘no name’ in this case) to change it. Confirm the change with the enter key.



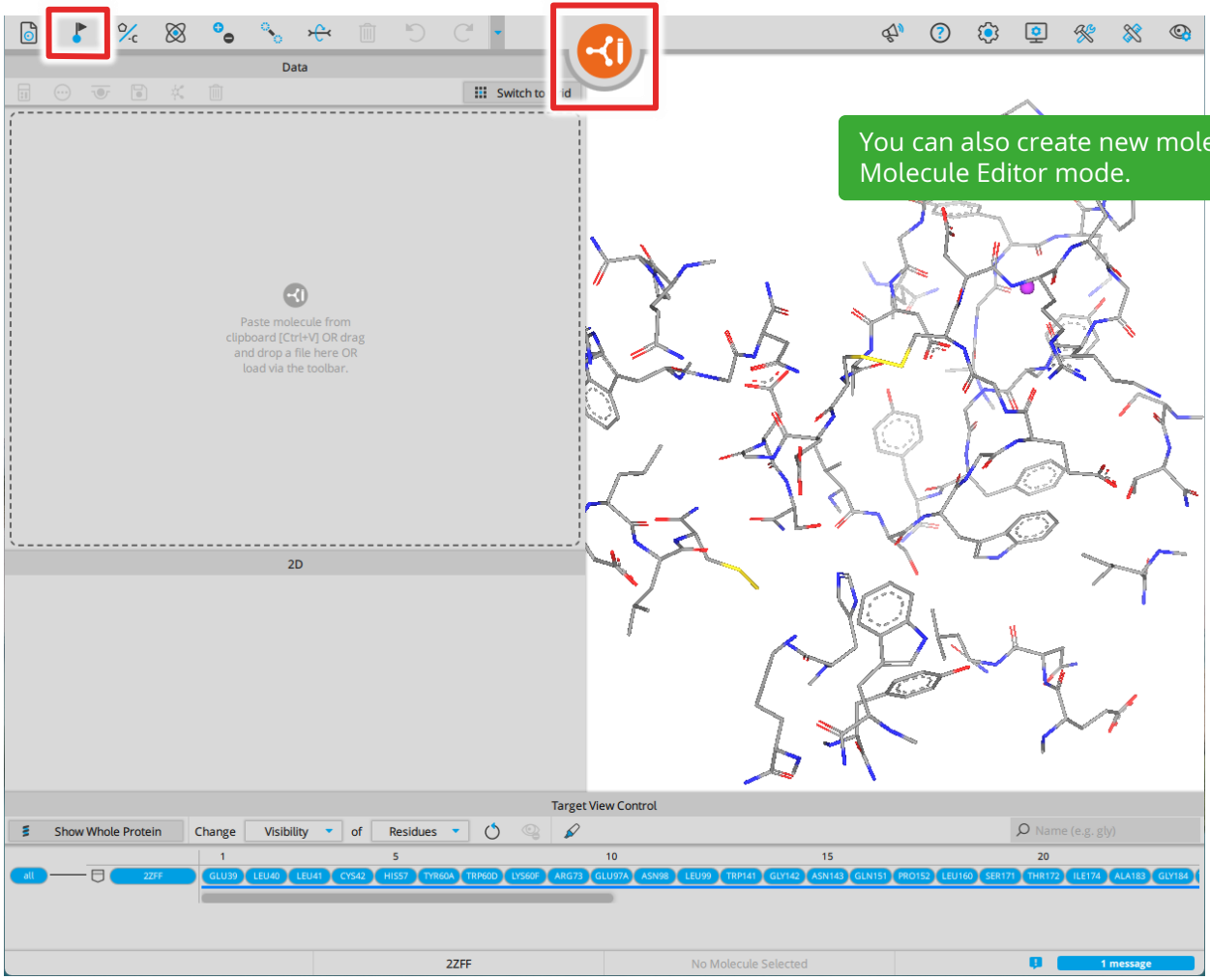
To transfer all of your compounds to another mode (e.g. to dock them in the Docking mode), click on the 'Checked' column and select 'Check all' to mark all molecules in the list.

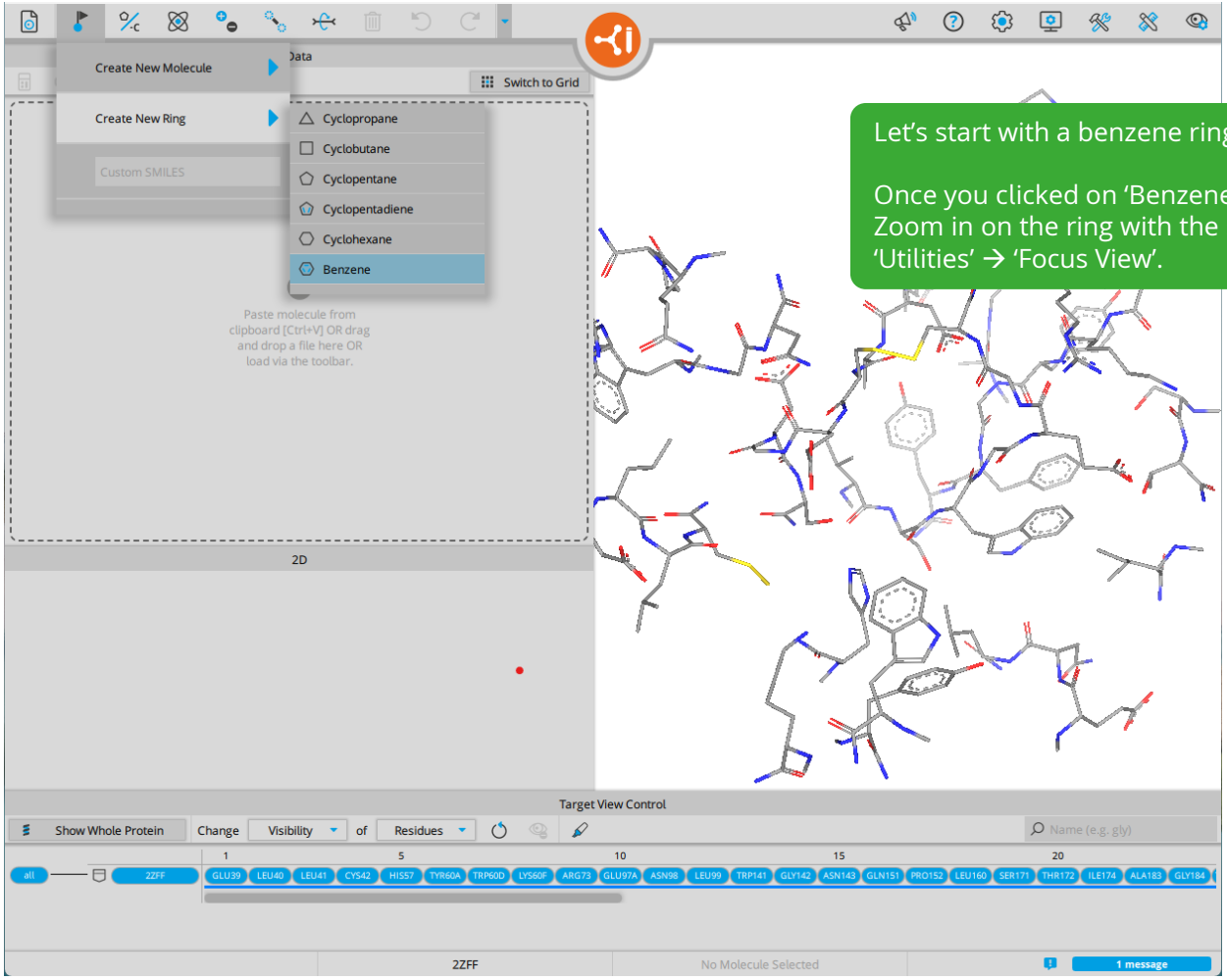
If you want to transfer only some of the molecules, check them individually in the column.

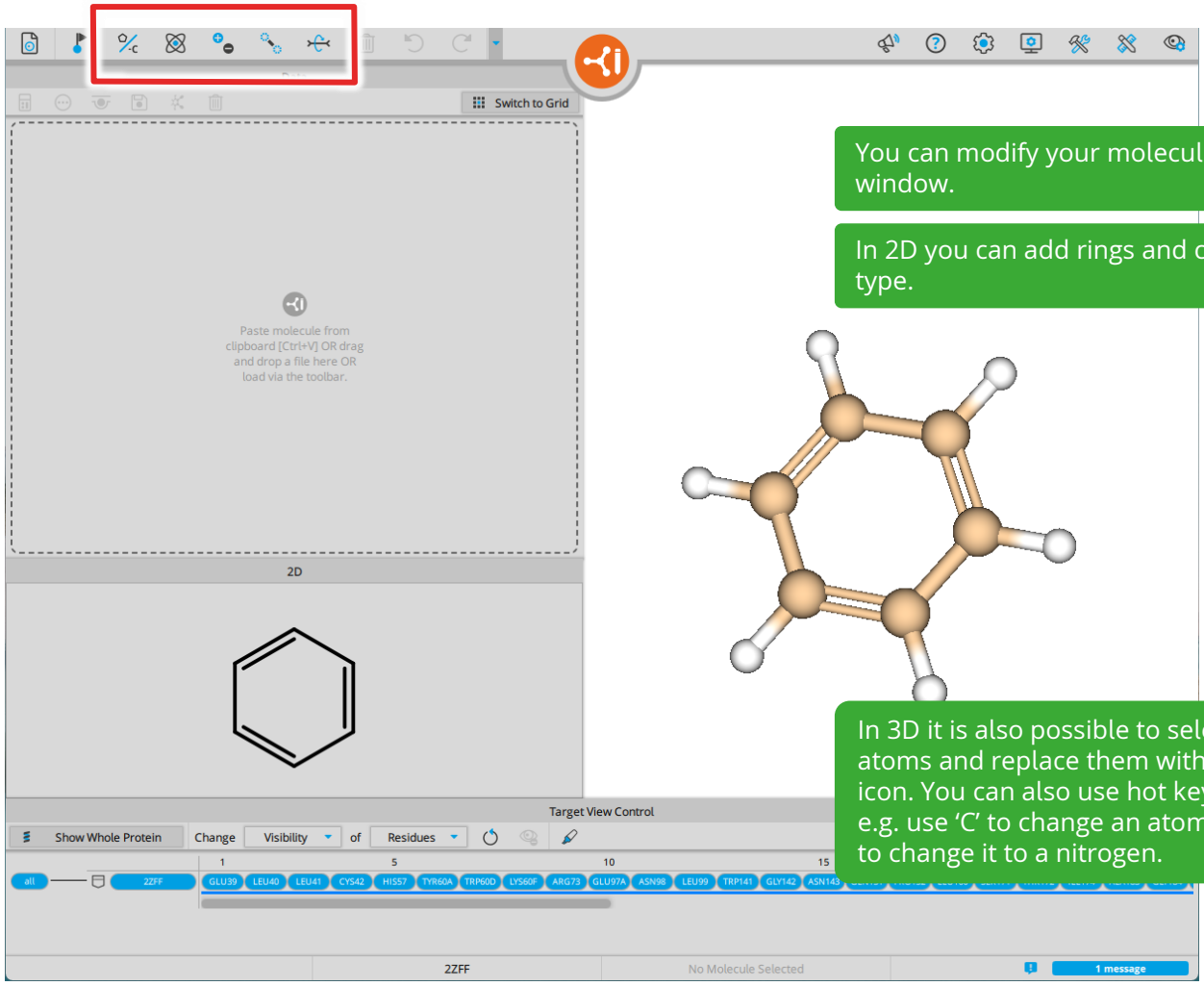


Click on 'Add checked molecules to mode' and select the mode of your choice to work with the molecules.
Since we want to dock them, we will select the **Docking mode on local machine**.

The docking procedure is explained in Section 3 (Docking).


Data
Switch to
Paste molecule from clipboard [Ctrl+V] OR drag and drop a file here OR load via the toolbar.
2D
You can also create new molecules in the Molecule Editor mode.
Target View Control
Show Whole Protein
Change
Visibility
of
Residues
Name (e.g. gly)
2ZFF
No Molecule Selected
1 message

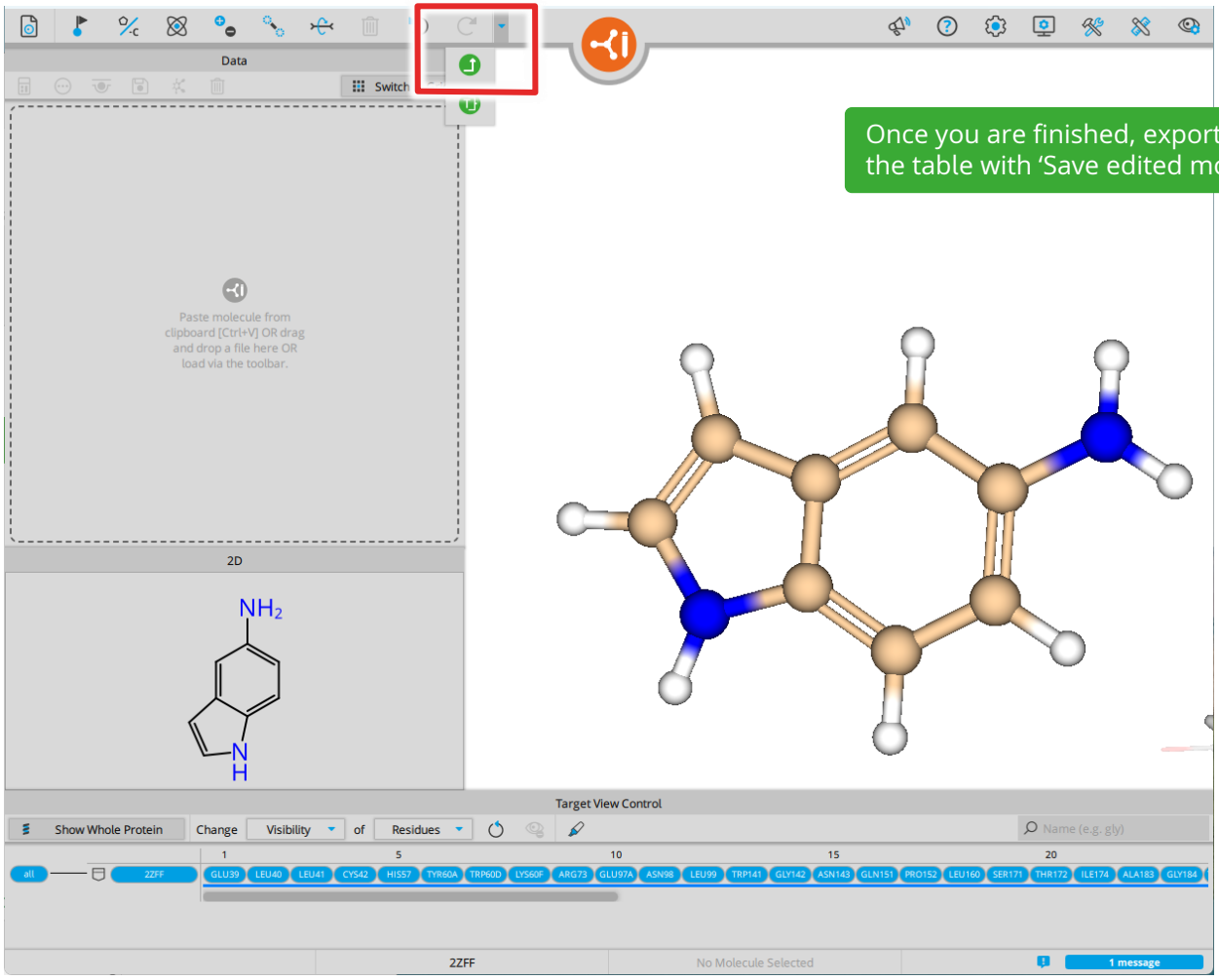

Create New Molecule
Create New Ring
Custom SMILES
Cyclopropane
Cyclobutane
Cyclopentane
Cyclopentadiene
Cyclohexane
Benzene
Switch to Grid
Paste molecule from clipboard [Ctrl+V] OR drag and drop a file here OR load via the toolbar.
2D
Let's start with a benzene ring.
Once you clicked on 'Benzene' a ring will appear. Zoom in on the ring with the space bar or via 'Utilities' → 'Focus View'.
Target View Control
Show Whole Protein
Change
Visibility
of
Residues
2ZFF
No Molecule Selected
1 message



You can modify your molecule in the 2D and 3D window.

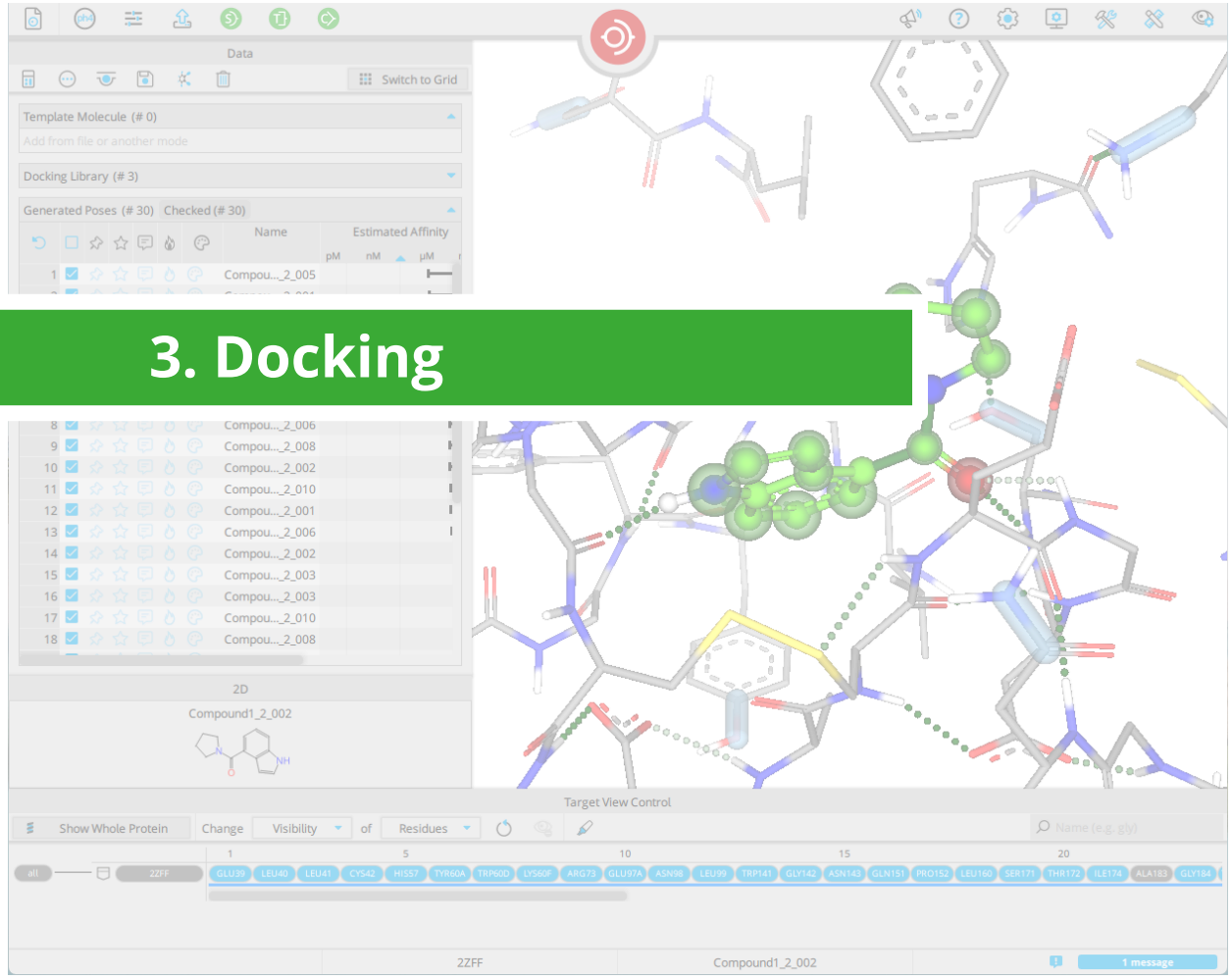
In 2D you can add rings and change the bond type.

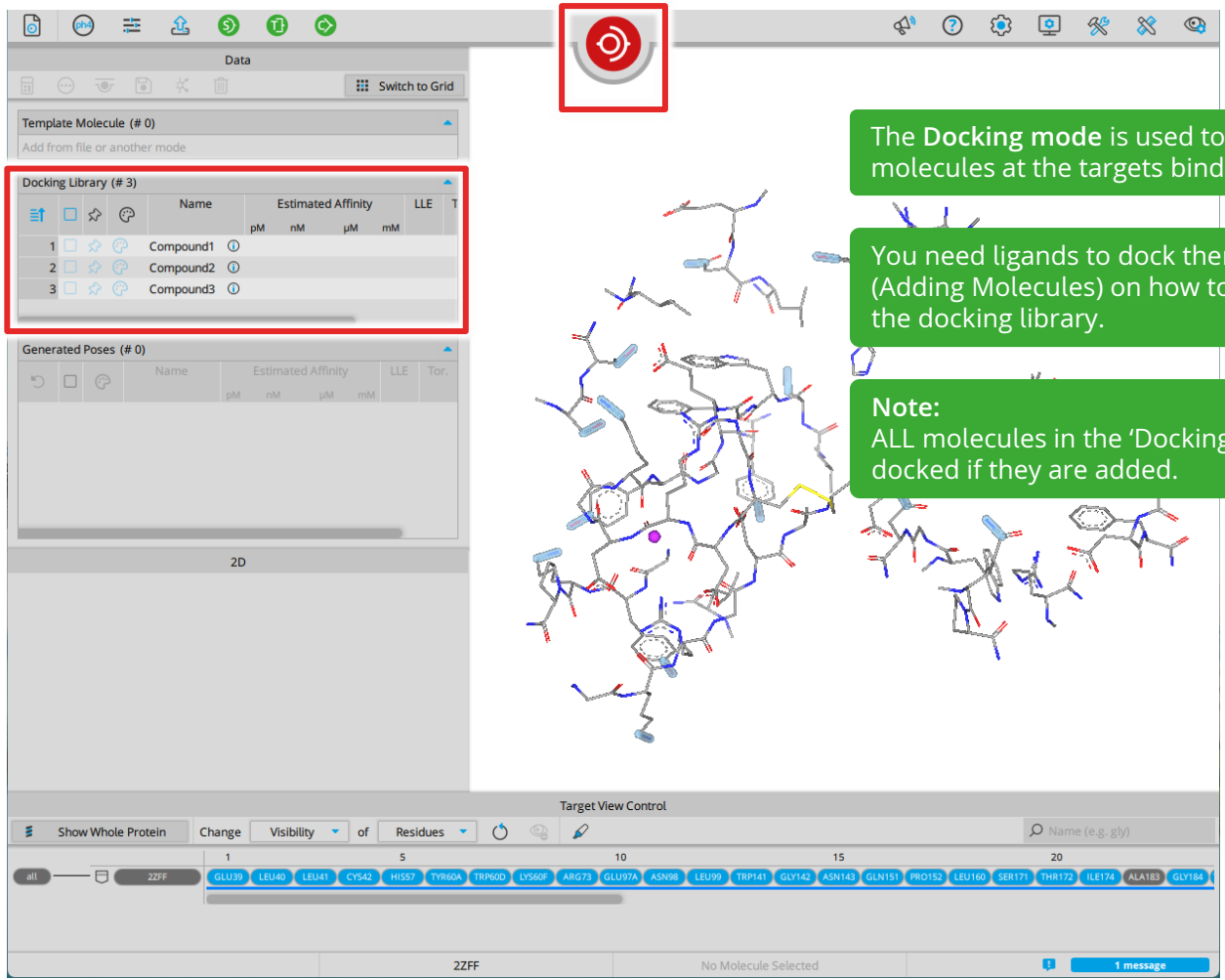
In 3D it is also possible to select the hydrogen atoms and replace them with 'Change element' icon. You can also use hot keys for elements, e.g. use 'C' to change an atom to a carbon or 'N' to change it to a nitrogen.



Once you are finished, export the molecule to the table with ‘Save edited molecules to table’.

3. Docking

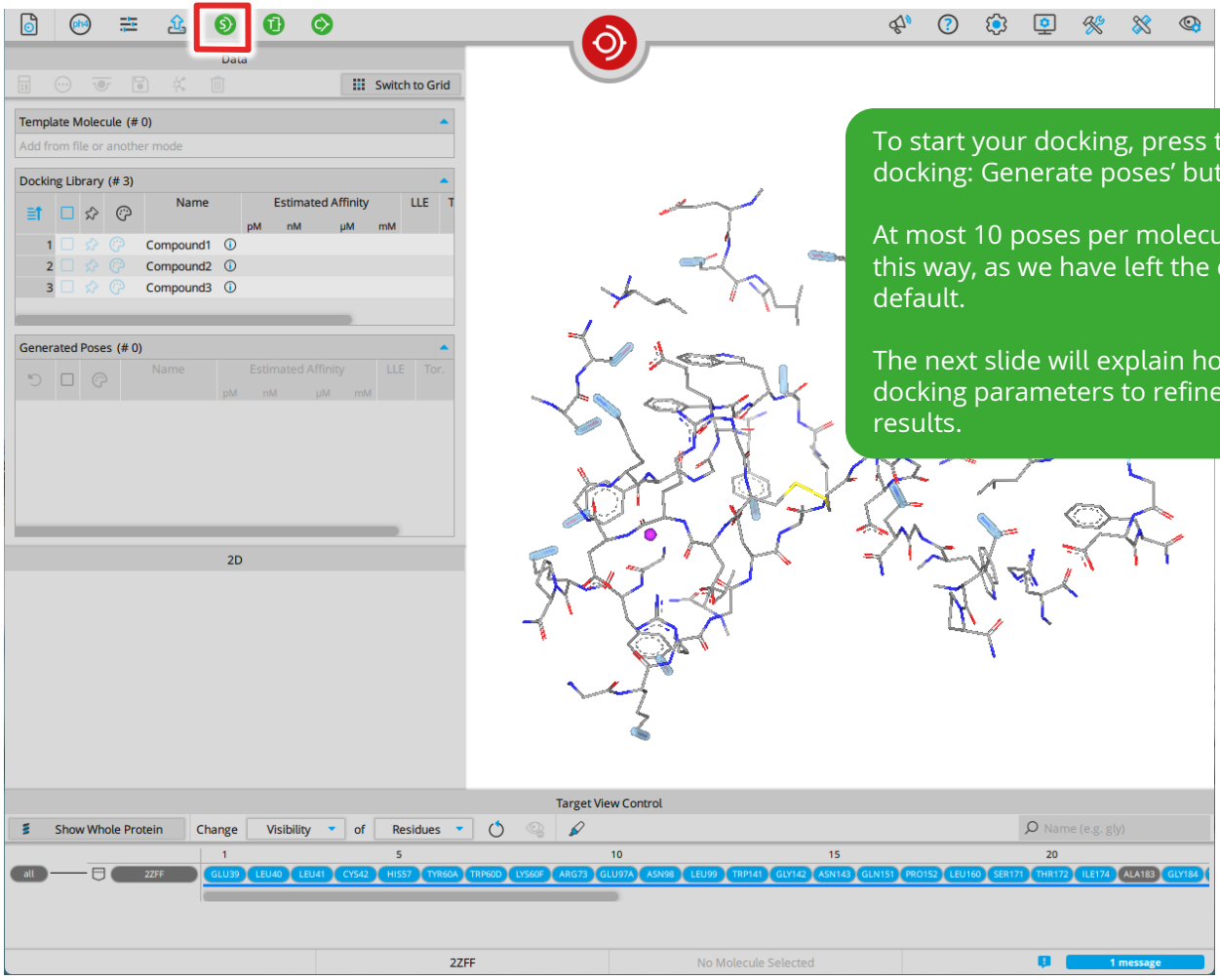

Data
Switch to Grid
Template Molecule (# 0)
Add from file or another mode
Docking Library (# 3)
Generated Poses (# 30)
Checked (# 30)
Name
Estimated Affinity
pM
nM
µM
1 Compou..._2_005
8 Compou..._2_006
9 Compou..._2_008
10 Compou..._2_002
11 Compou..._2_010
12 Compou..._2_001
13 Compou..._2_006
14 Compou..._2_002
15 Compou..._2_003
16 Compou..._2_003
17 Compou..._2_010
18 Compou..._2_008
2D
Compound1_2_002
Target View Control
Show Whole Protein
Change
Visibility
of
Residues
Name (e.g. gly)
all
2ZFF
GLU39 LEU40 LEU41 CYS42 HIS57 TYR60A TRP60D LYS60F ARG73 GLU97A ASN98 LEU99 TRP141 GLY142 ASN143 GLN151 PRO152 LEU160 SER171 THR172 ILE174 ALA183 GLY184
2ZFF
Compound1_2_002
1 message



The **Docking mode** is used to place (= dock) molecules at the targets binding site.

You need ligands to dock them. See Section 2 (Adding Molecules) on how to add molecules to the docking library.

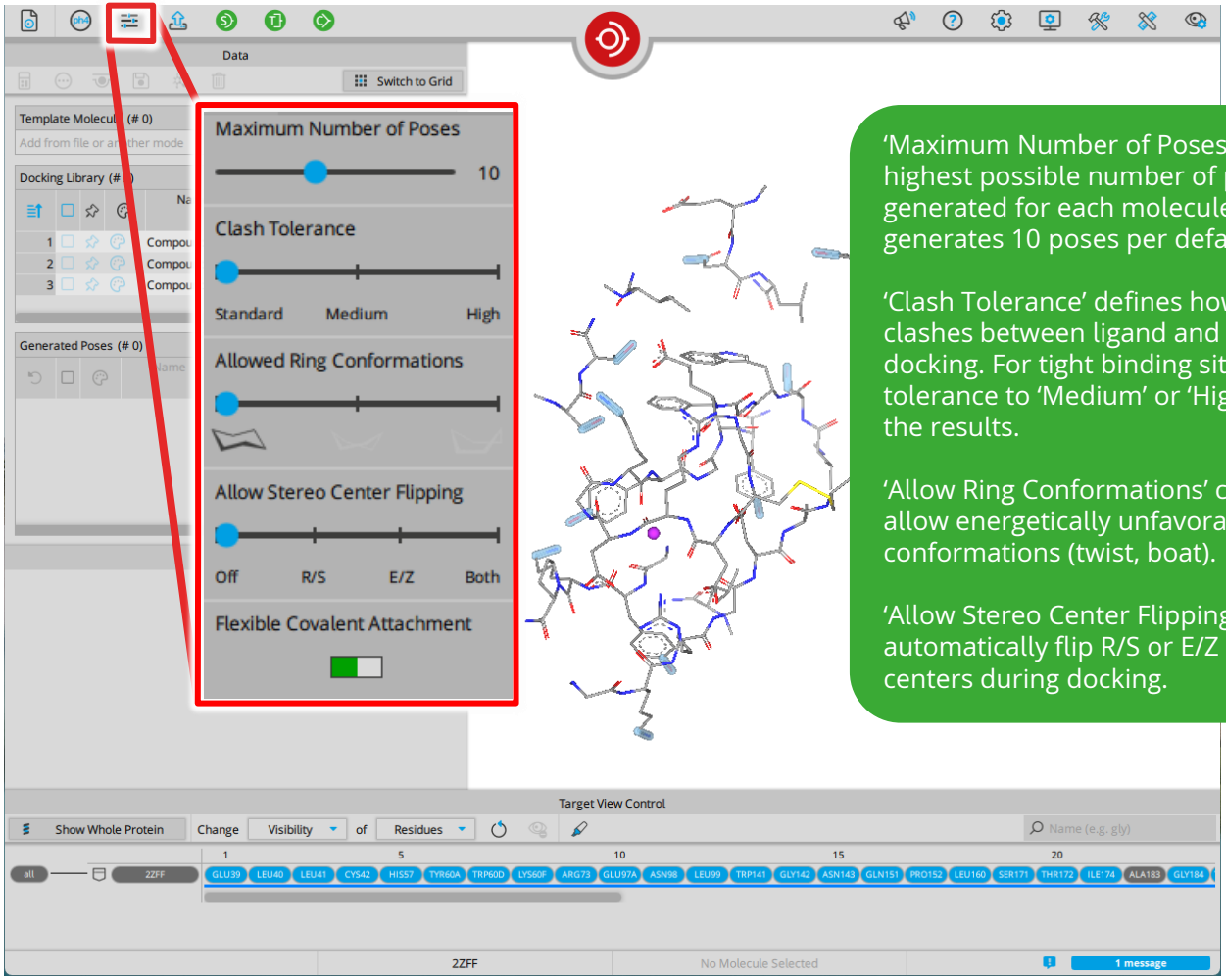
Note:
ALL molecules in the 'Docking library' will be docked if they are added.



To start your docking, press the 'Standard docking: Generate poses' button.

At most 10 poses per molecule are generate this way, as we have left the docking settings on default.

The next slide will explain how to adjust docking parameters to refine your docking results.

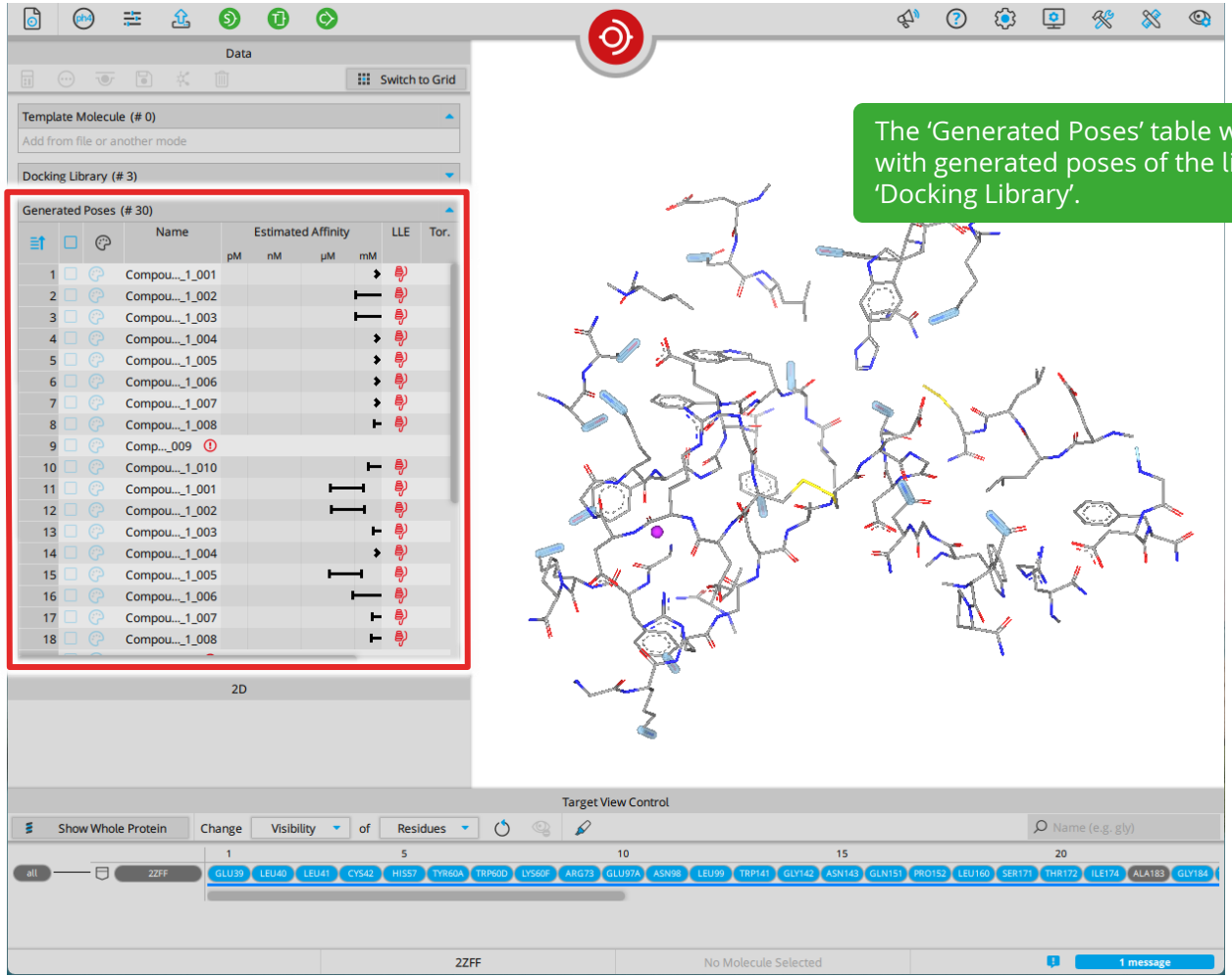


'Maximum Number of Poses' defines the highest possible number of poses that will be generated for each molecule. SeeSAR generates 10 poses per default.

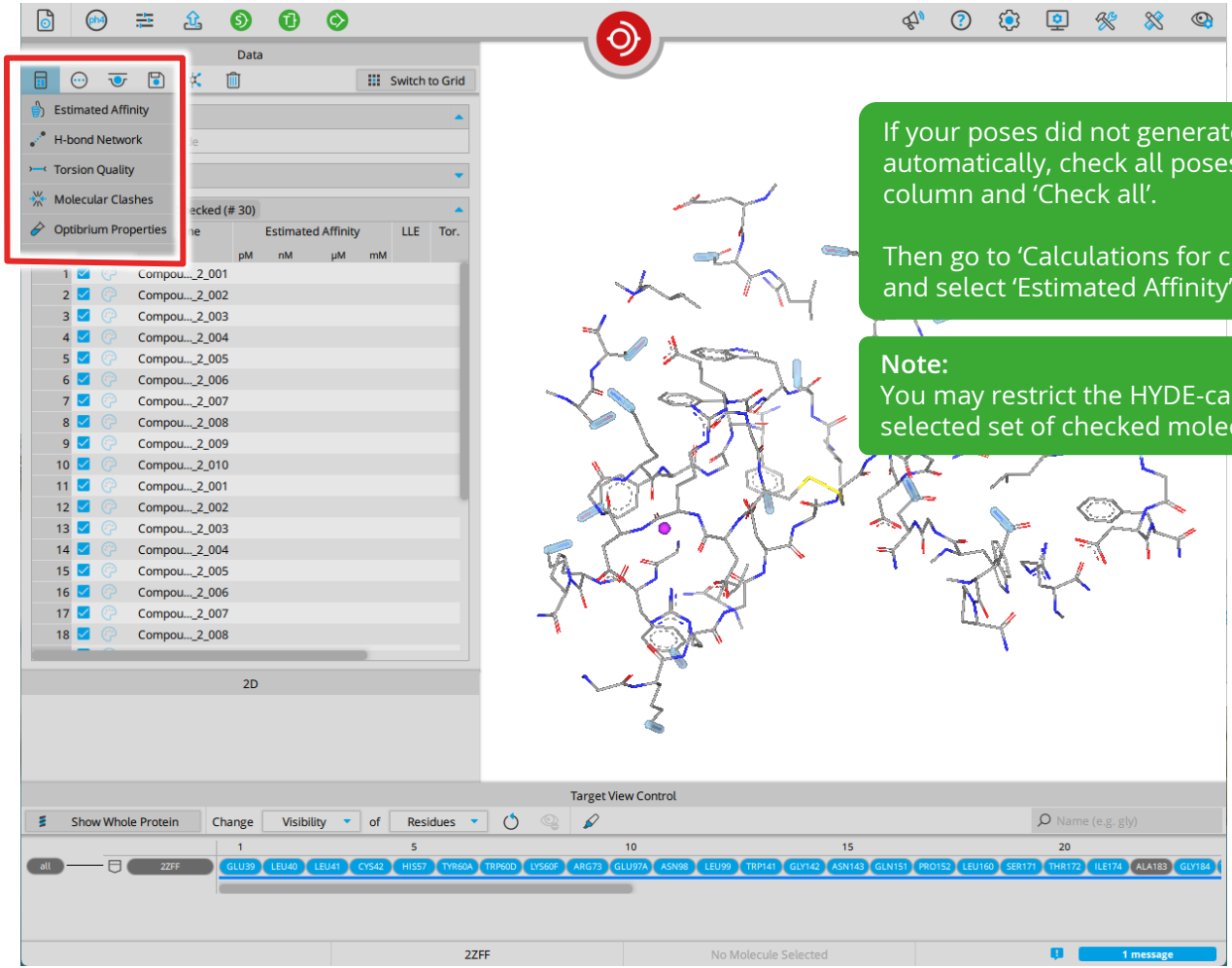
'Clash Tolerance' defines how SeeSAR handles clashes between ligand and target during docking. For tight binding sites increase of the tolerance to 'Medium' or 'High' may improve the results.

'Allow Ring Conformations' can be used to allow energetically unfavorable ring conformations (twist, boat).

'Allow Stereo Center Flipping' can be used to automatically flip R/S or E/Z or both stereo centers during docking.



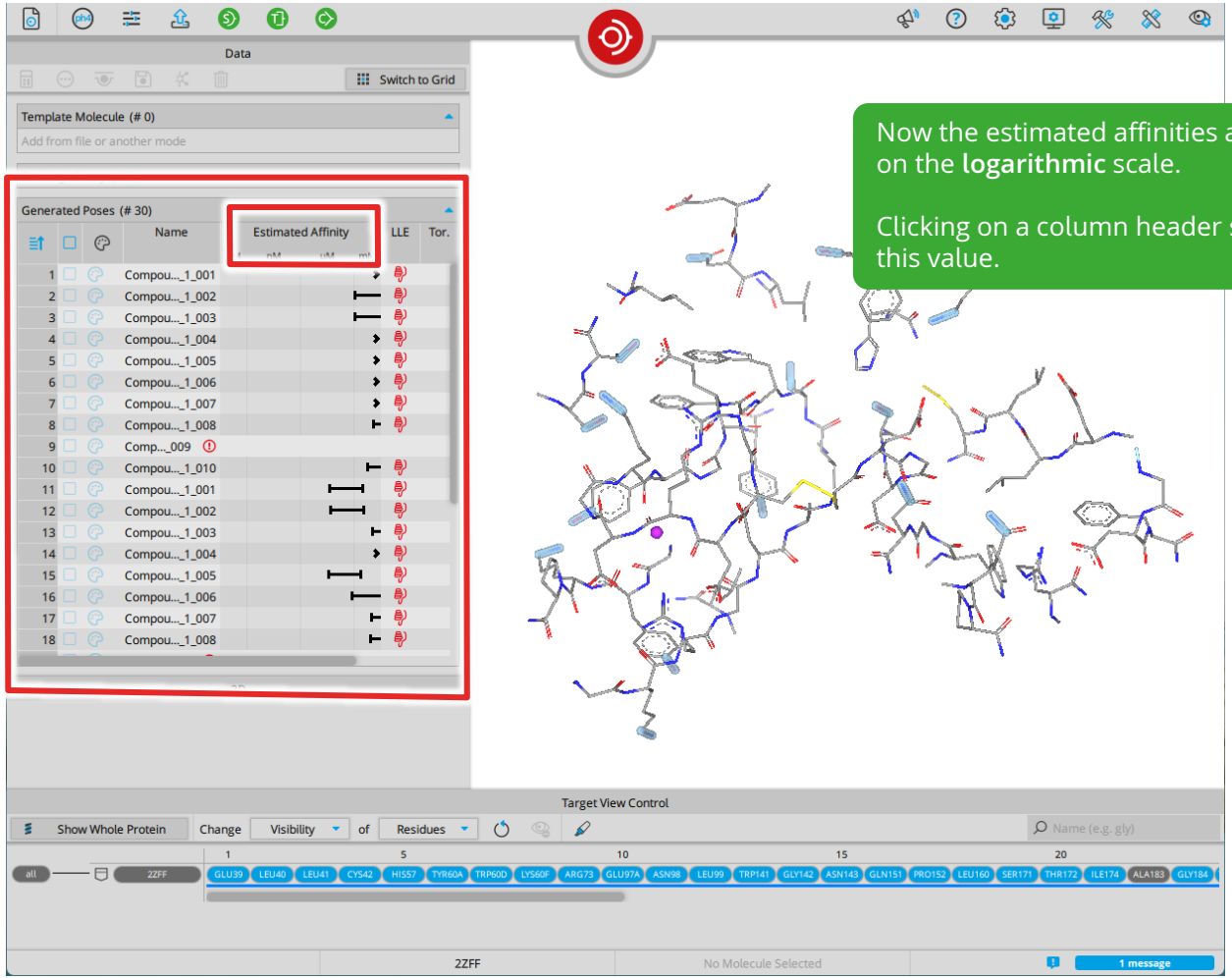
The ‘Generated Poses’ table will be populated with generated poses of the ligands from ‘Docking Library’.



If your poses did not generate affinity automatically, check all poses with the 'Checked' column and 'Check all'.

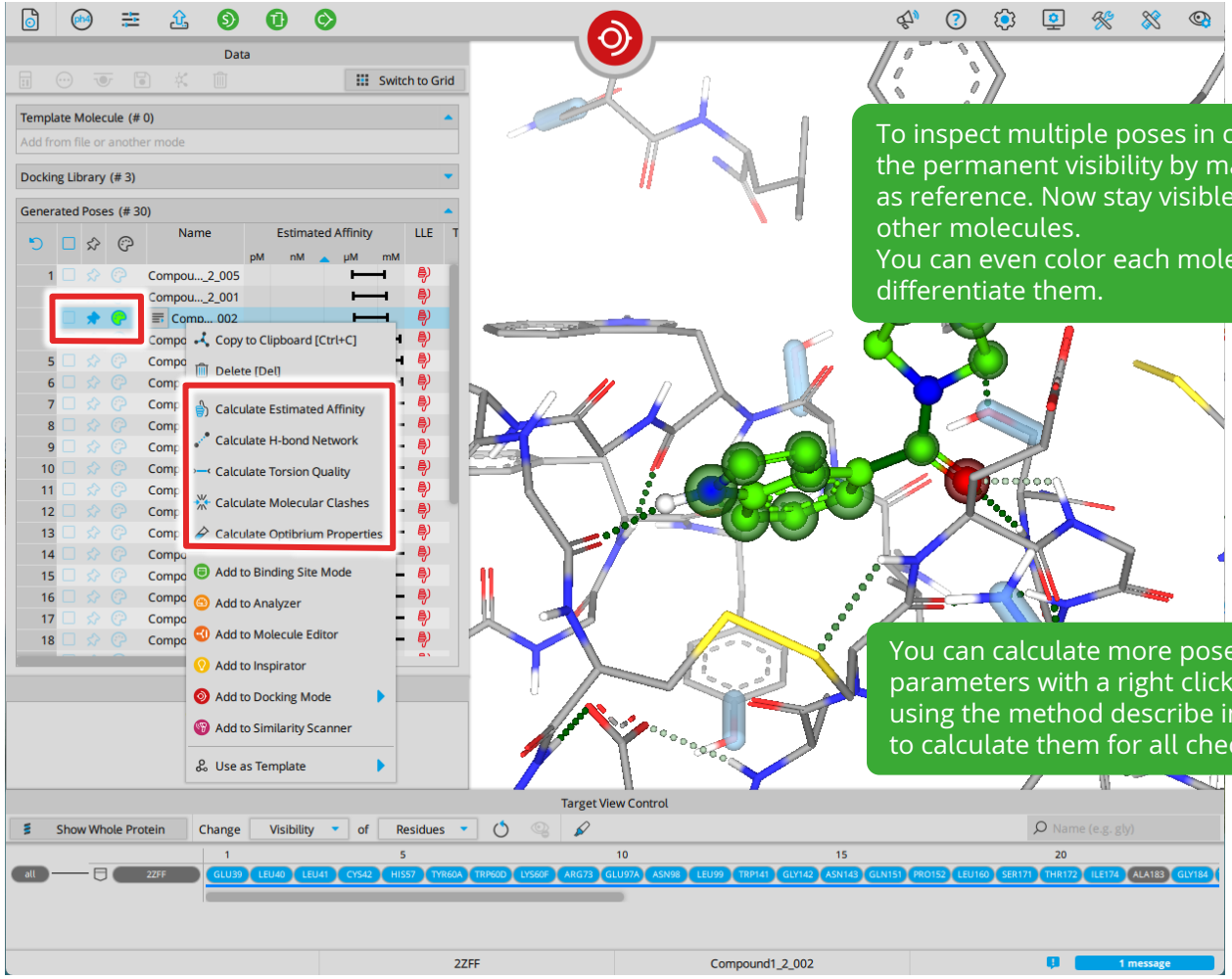
Then go to 'Calculations for checked molecules' and select 'Estimated Affinity'.

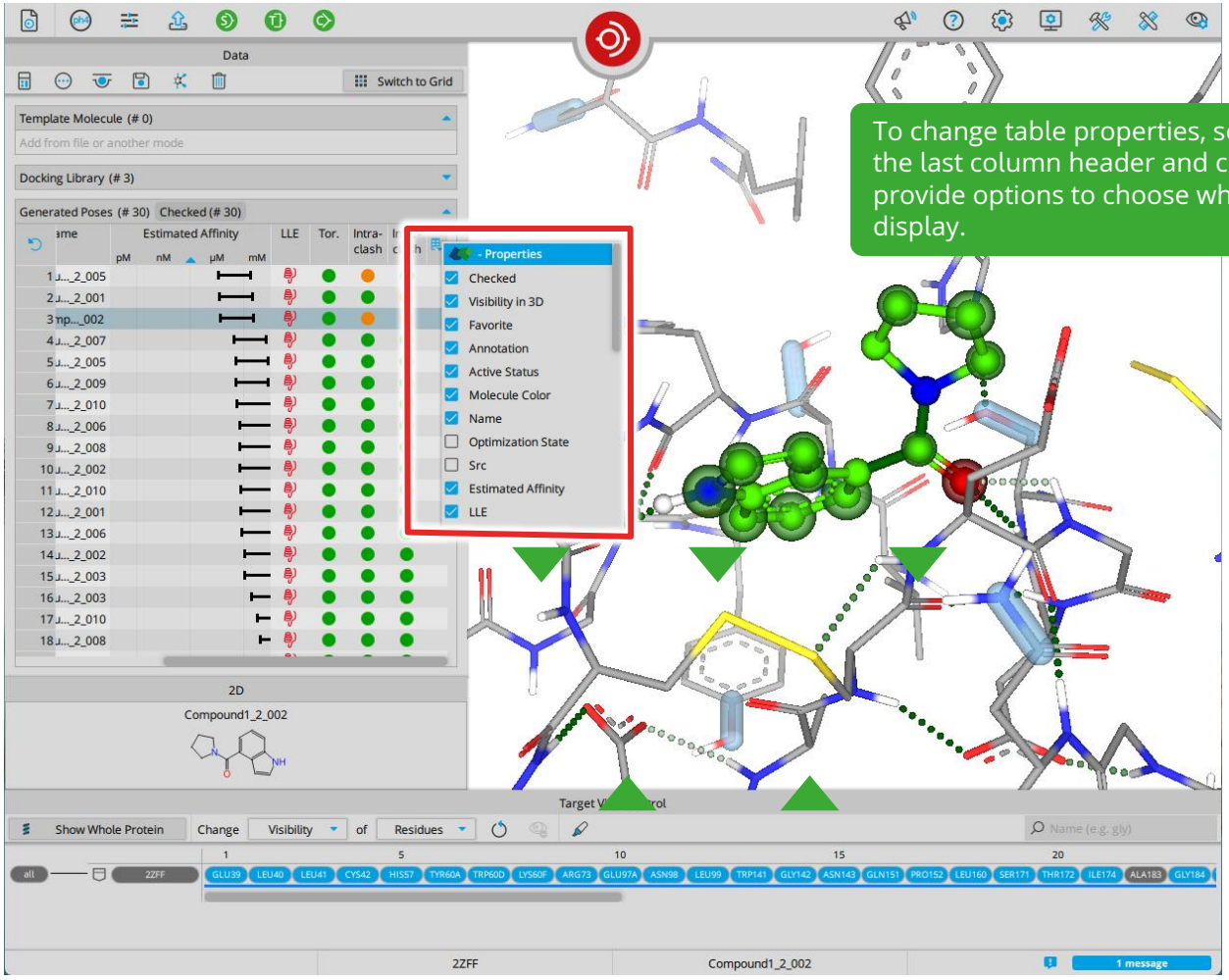
Note:
You may restrict the HYDE-calculation to a pre-selected set of checked molecules.

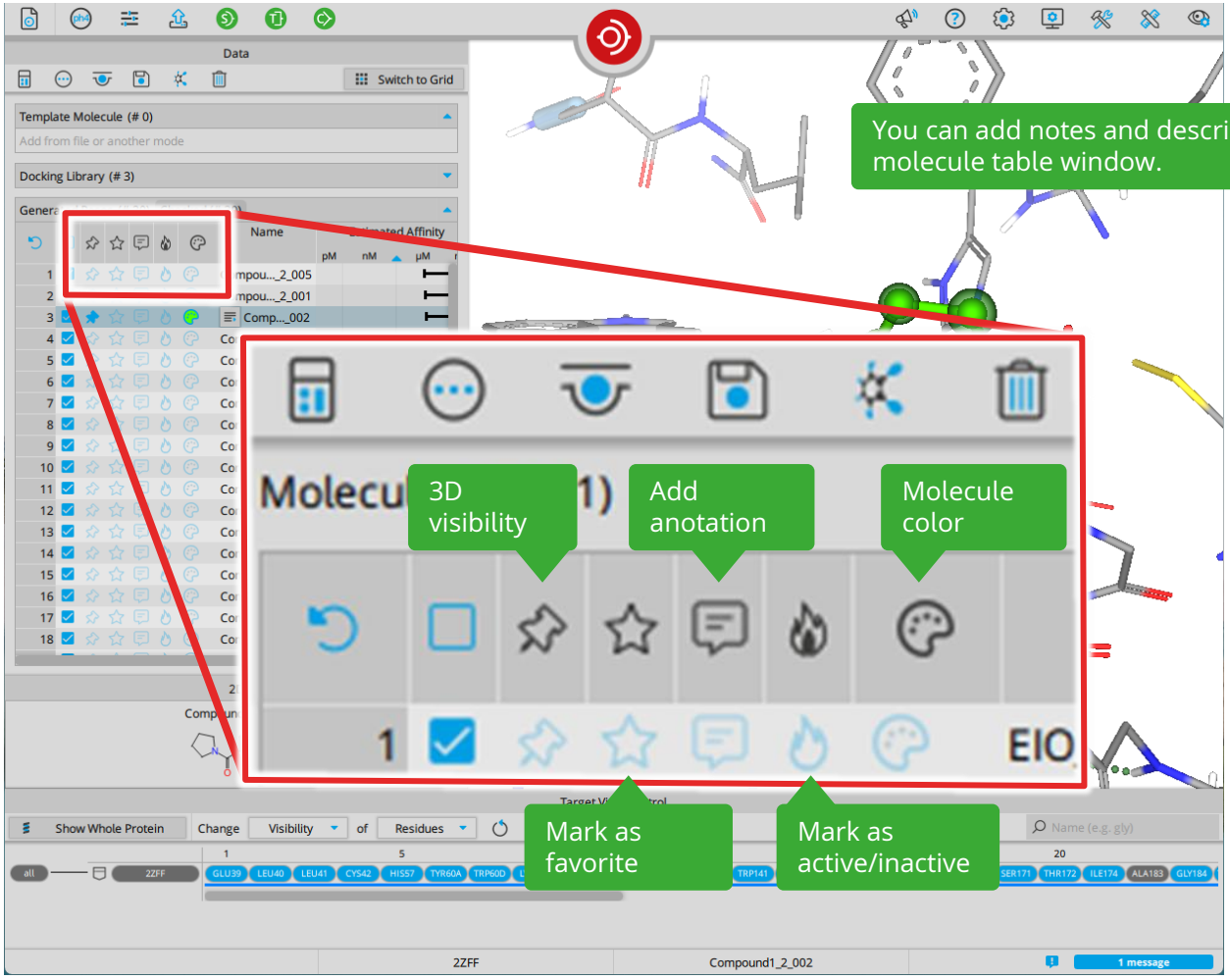


Now the estimated affinities appear as a range on the **logarithmic** scale.

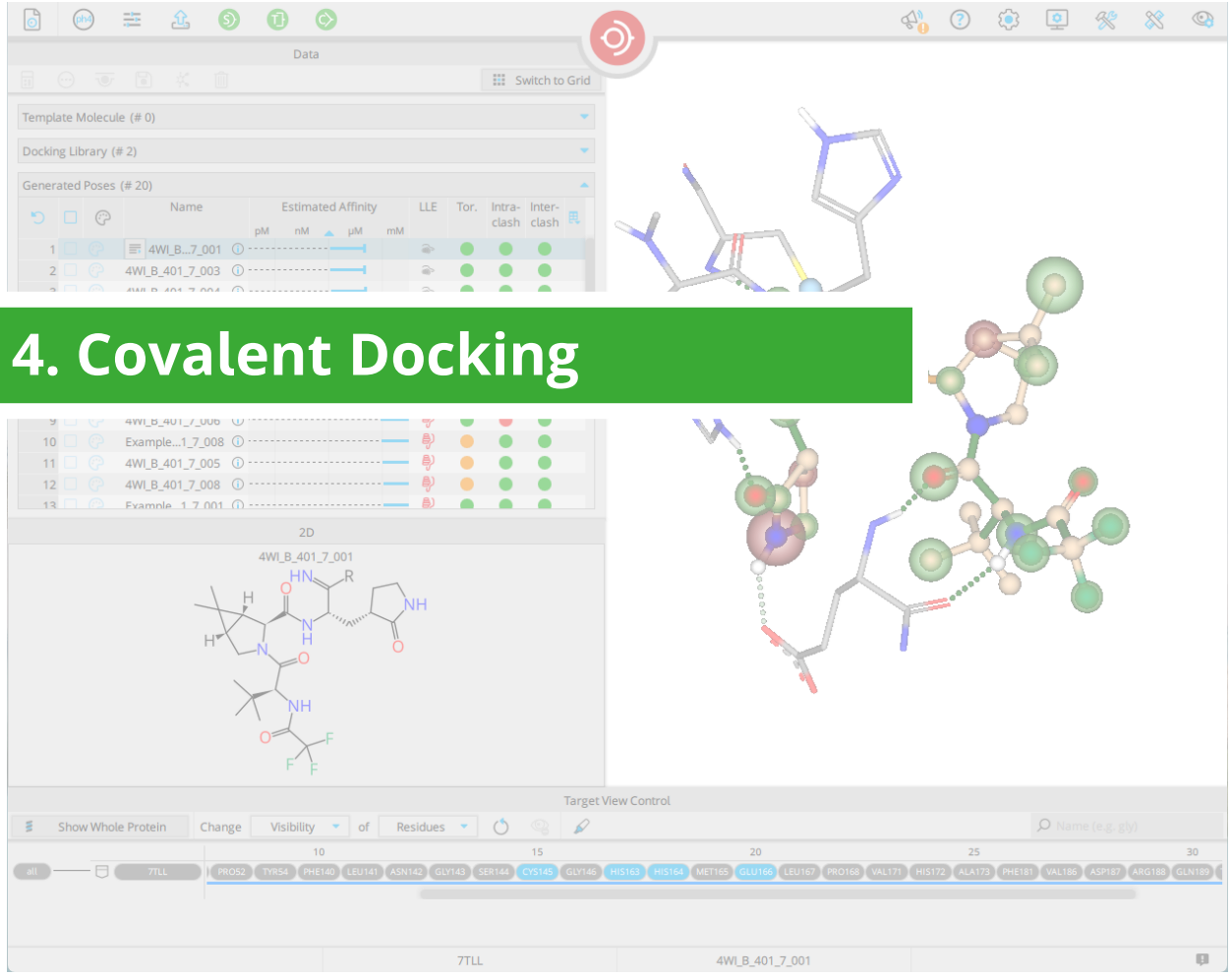
Clicking on a column header sorts according to this value.

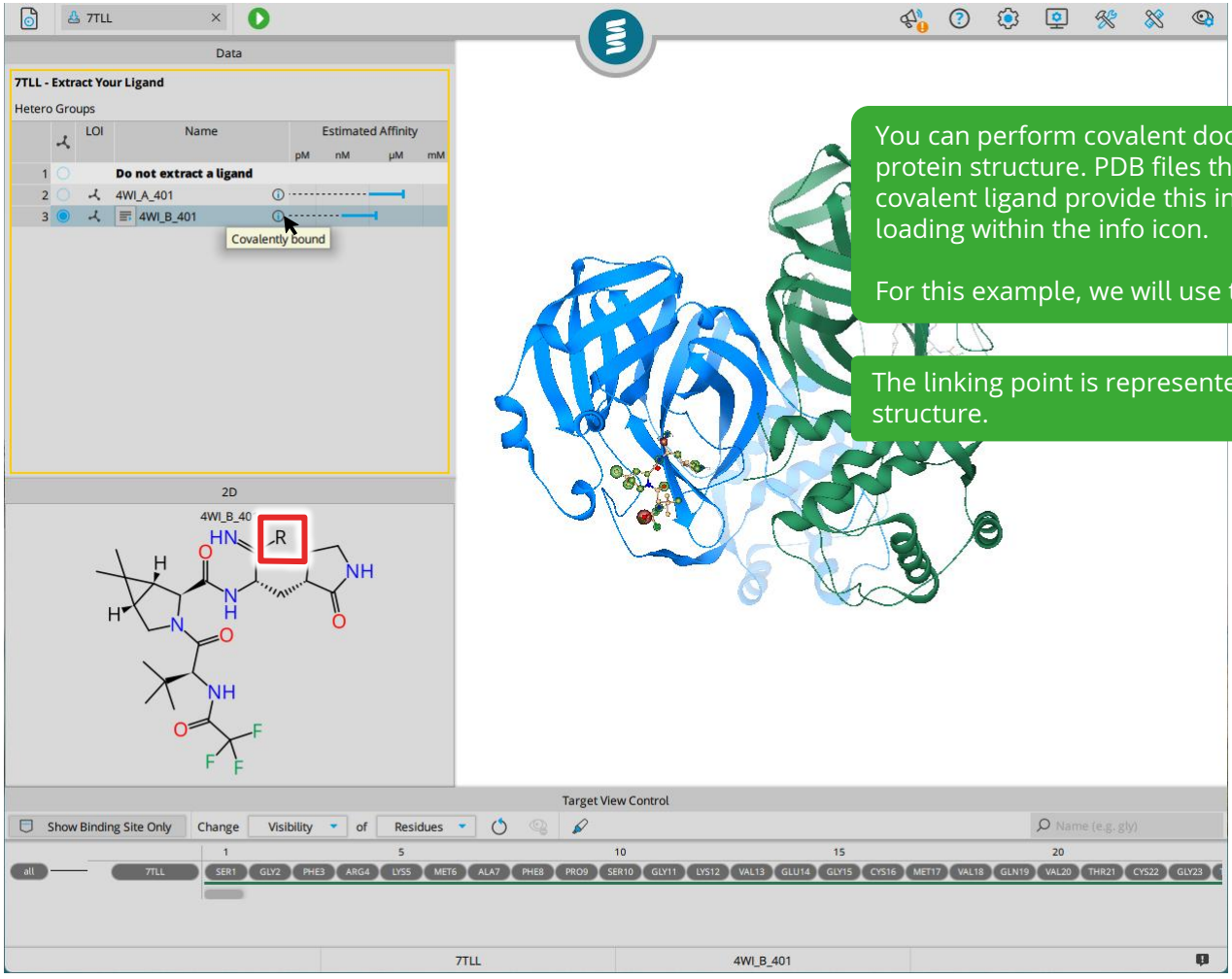

Data
Switch to Grid
Template Molecule (# 0)
Add from file or another mode
Docking Library (# 3)
Generated Poses (# 30)
Name
Estimated Affinity
LLE
Copy to Clipboard [Ctrl+C]
Delete [Del]
Calculate Estimated Affinity
Calculate H-bond Network
Calculate Torsion Quality
Calculate Molecular Clashes
Calculate Optibrium Properties
Add to Binding Site Mode
Add to Analyzer
Add to Molecule Editor
Add to Inspirator
Add to Docking Mode
Add to Similarity Scanner
Use as Template
To inspect multiple poses in comparison, toggle the permanent visibility by marking a molecule as reference. Now stay visible as you select other molecules.
You can even color each molecule to differentiate them.
You can calculate more pose assessment parameters with a right click on a molecule, or using the method describe in the previous slides to calculate them for all checked molecules.
Target View Control
Show Whole Protein
Change
Visibility
of
Residues
2ZFF
Compound1_2_002
1 message


Data
Switch to Grid
Template Molecule (# 0)
Add from file or another mode
Docking Library (# 3)
Generated Poses (# 30)
Checked (# 30)
Estimated Affinity
LLE
Tor.
Intra-clash
- Properties
Checked
Visibility in 3D
Favorite
Annotation
Active Status
Molecule Color
Name
Optimization State
Src
Estimated Affinity
LLE
2D
Compound1_2_002
To change table properties, scroll horizontally to the last column header and click on it. This will provide options to choose which columns to display.
Show Whole Protein
Change
Visibility
of
Residues
2ZFF
Compound1_2_002
1 message


You can add notes and descriptors in the molecule table window.
3D visibility
Add anotation
Molecule color
Mark as favorite
Mark as active/inactive
Data
Switch to Grid
Template Molecule (# 0)
Add from file or another mode
Docking Library (# 3)
Name
Show Whole Protein
Change
Visibility
of
Residues
2ZFF
Compound1_2_002
1 message

4. Covalent Docking

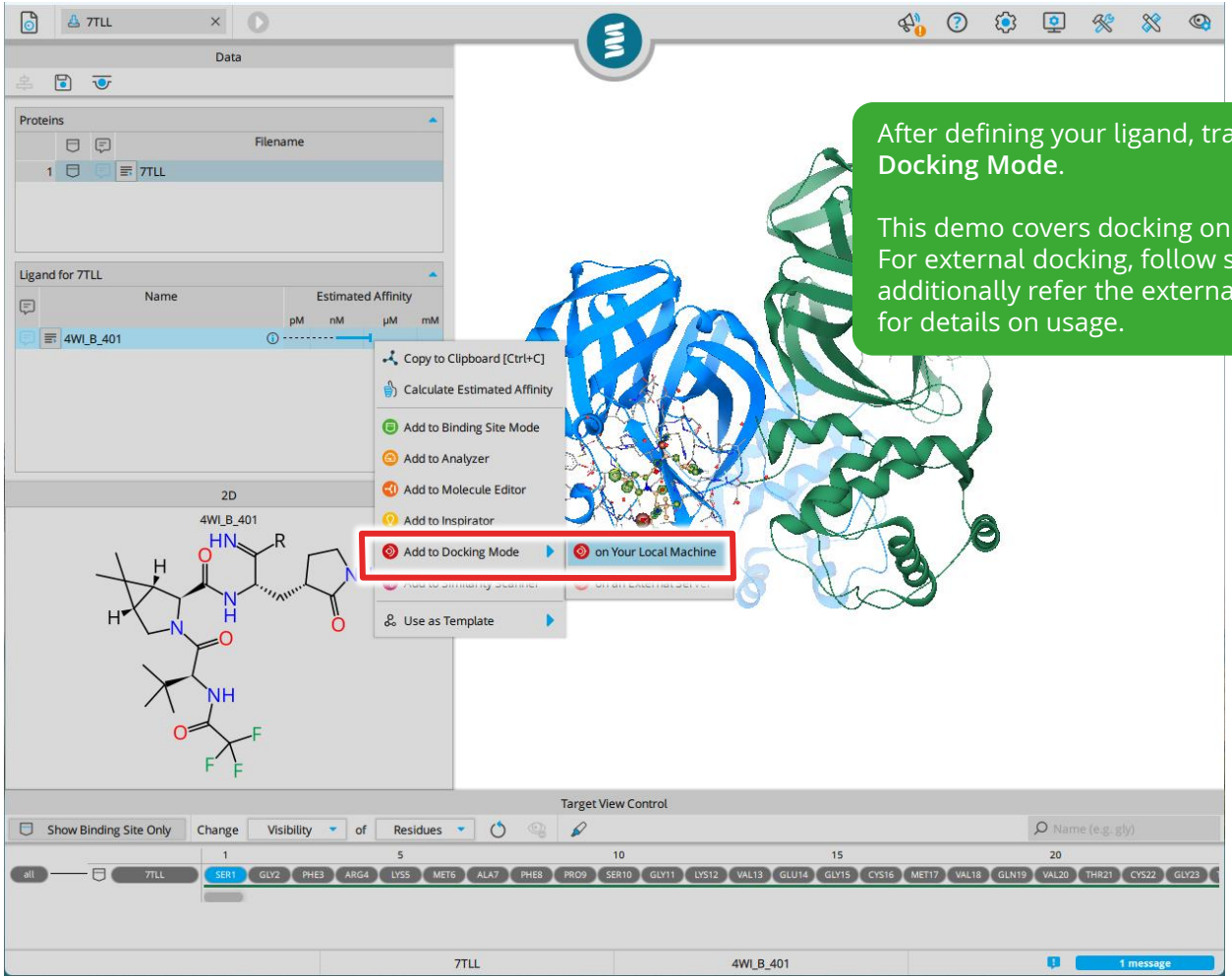




You can perform covalent docking at any PDB protein structure. PDB files that contain a covalent ligand provide this information upon loading within the info icon.

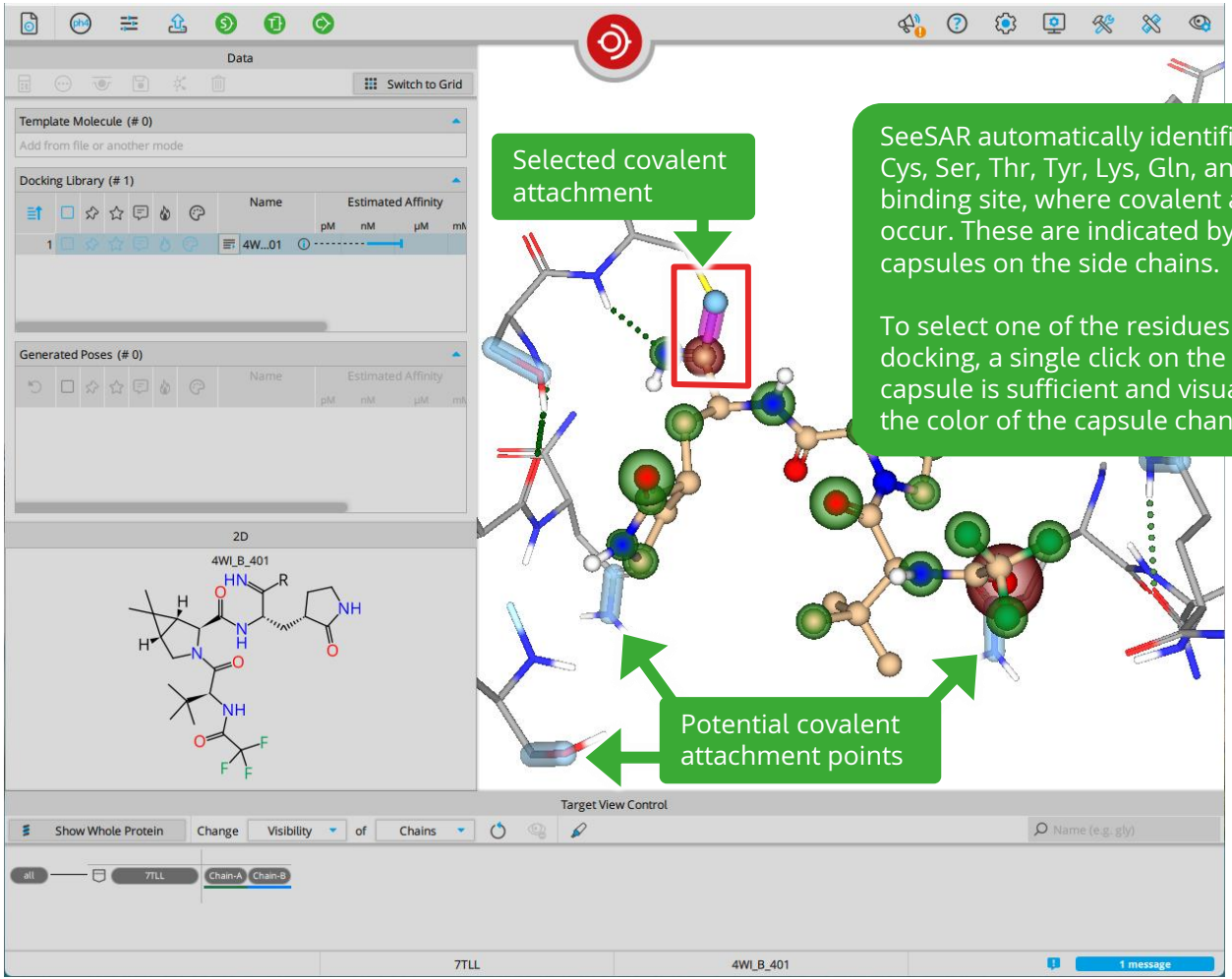
For this example, we will use the PDB **7TLL**.

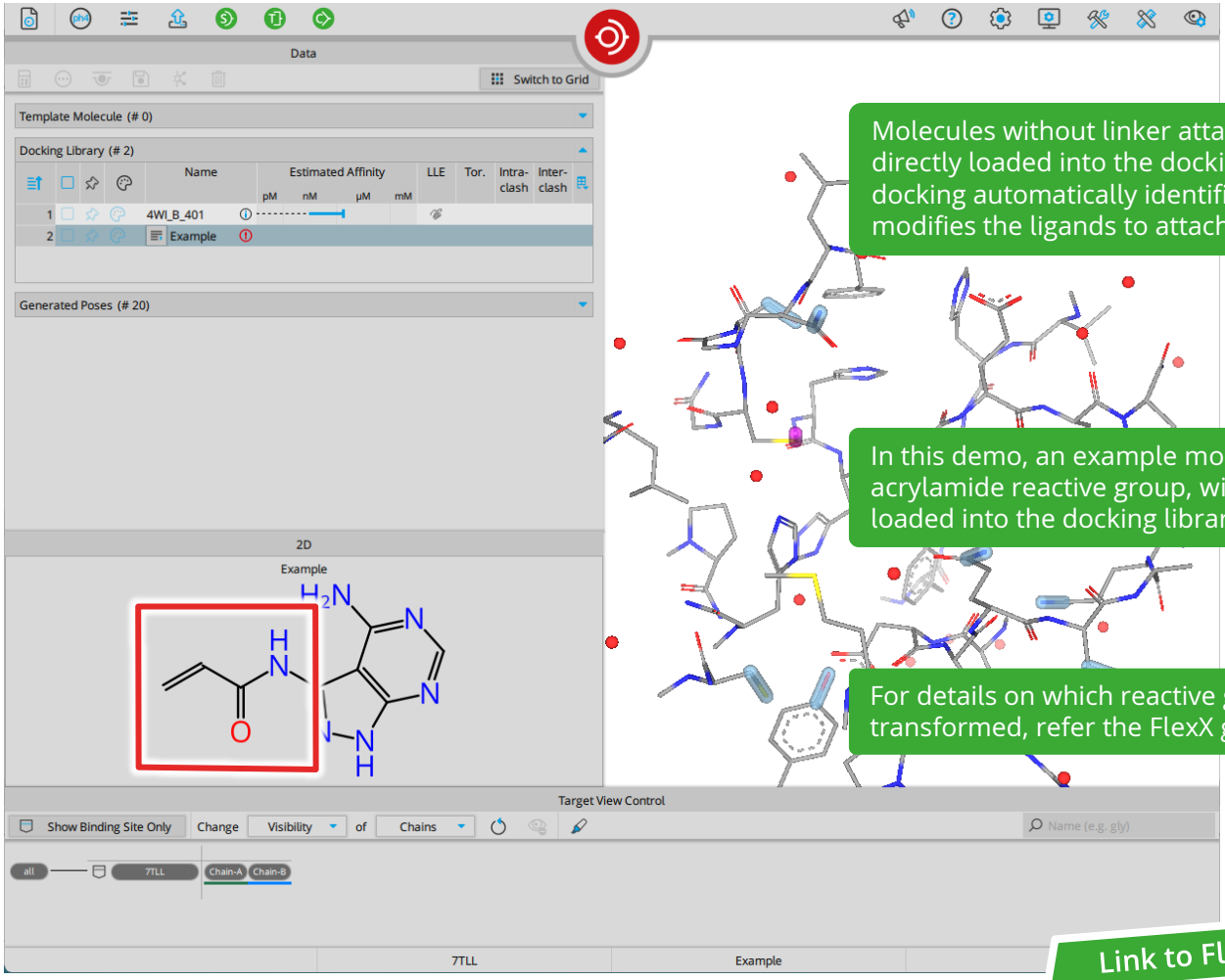
The linking point is represented as **R** in the 2D structure.



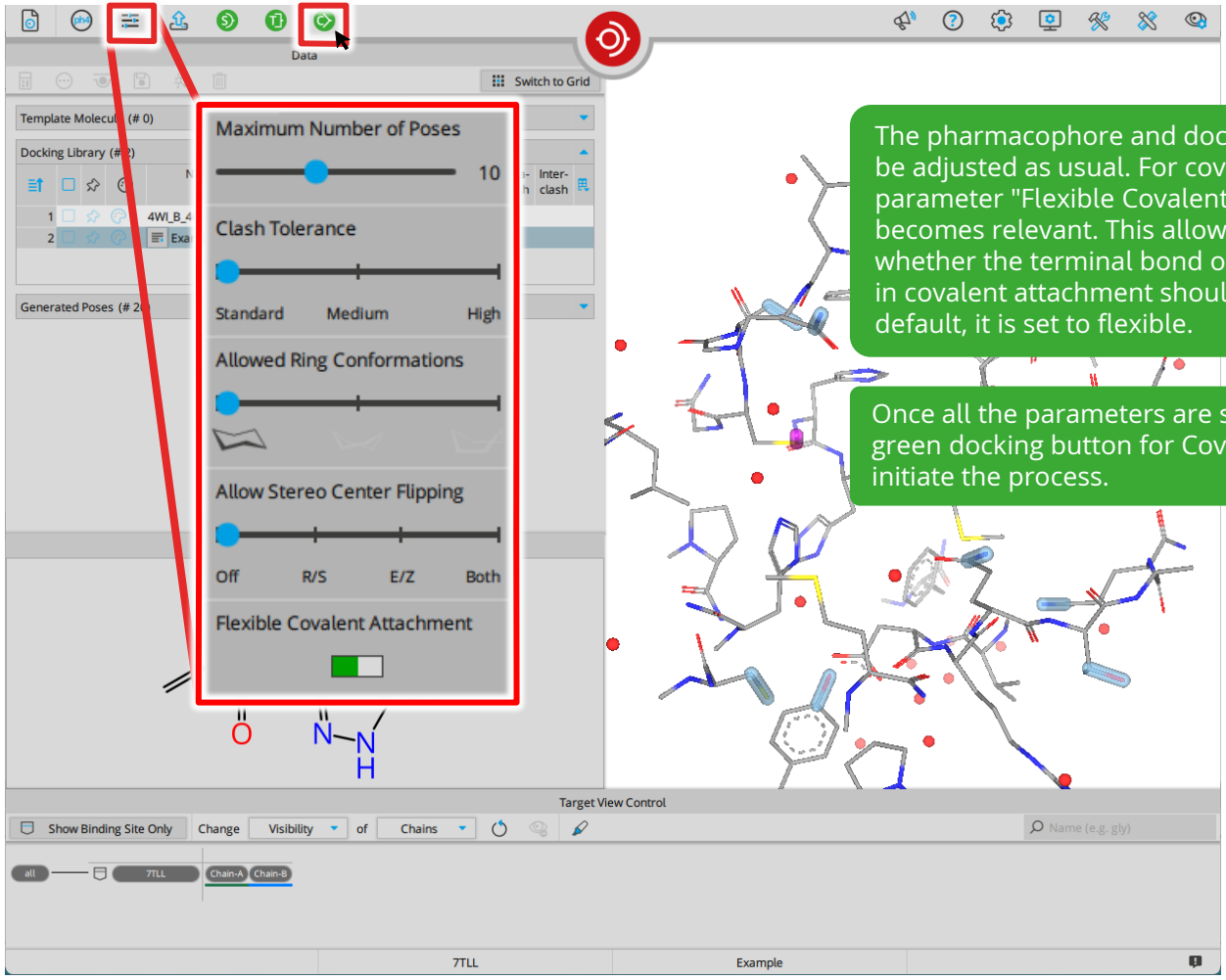
After defining your ligand, transfer it to the **Docking Mode**.

This demo covers docking on a local machine. For external docking, follow similar steps and additionally refer the external docking section for details on usage.


Data
Switch to Grid
Template Molecule (# 0)
Add from file or another mode
Docking Library (# 1)
Name
Estimated Affinity
4W...01
Generated Poses (# 0)
2D
4WI_B_401
Selected covalent attachment
Potential covalent attachment points
SeeSAR automatically identifies the residues Cys, Ser, Thr, Tyr, Lys, Gln, and Asn within the binding site, where covalent attachment may occur. These are indicated by blue translucent capsules on the side chains.
To select one of the residues for covalent docking, a single click on the corresponding capsule is sufficient and visually indicated by the color of the capsule changing to pink.
Target View Control
Show Whole Protein
Change
Visibility
of
Chains
all
7TLL
Chain-A
Chain-B
7TLL
4WI_B_401
1 message

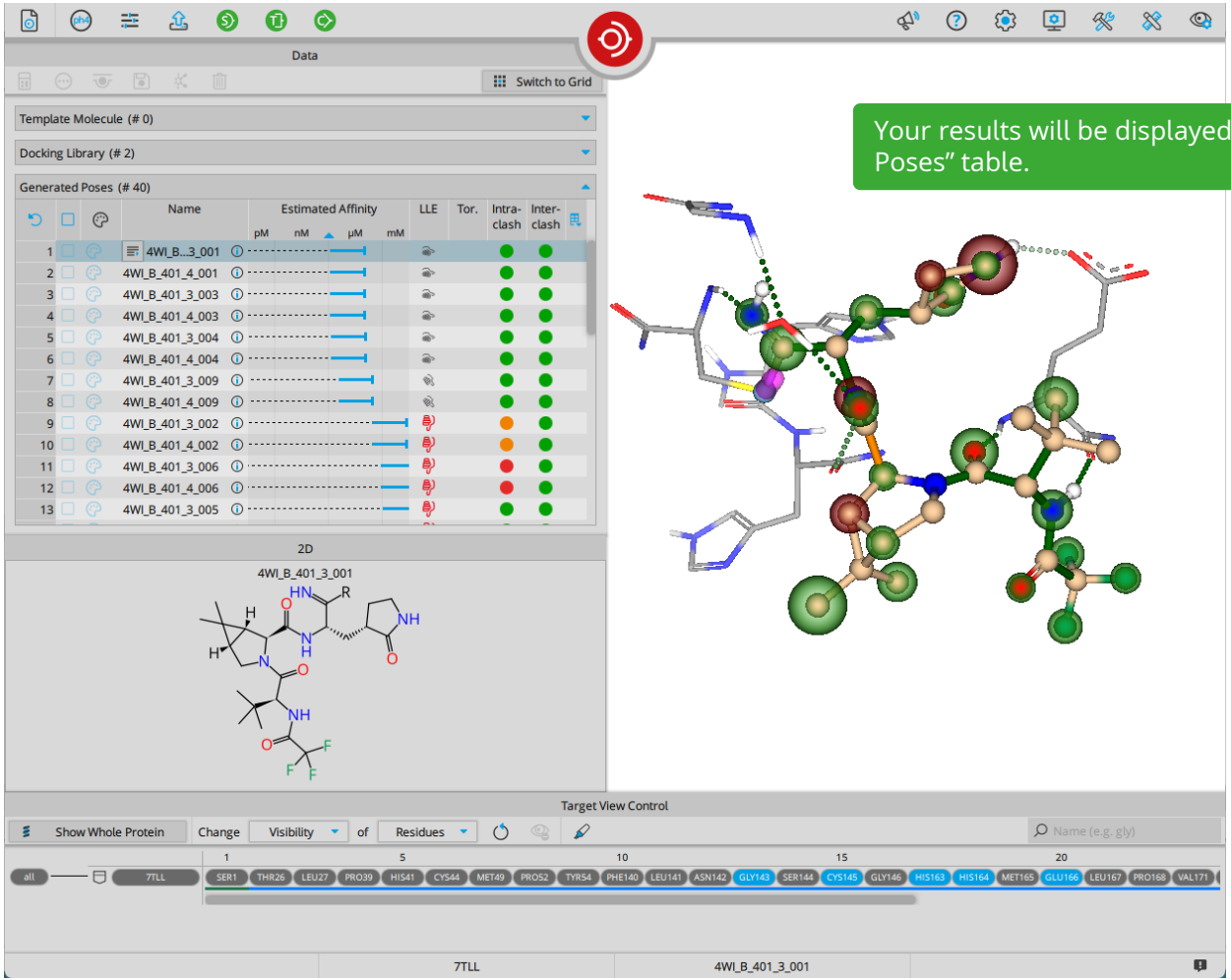


Link to FlexX Guide

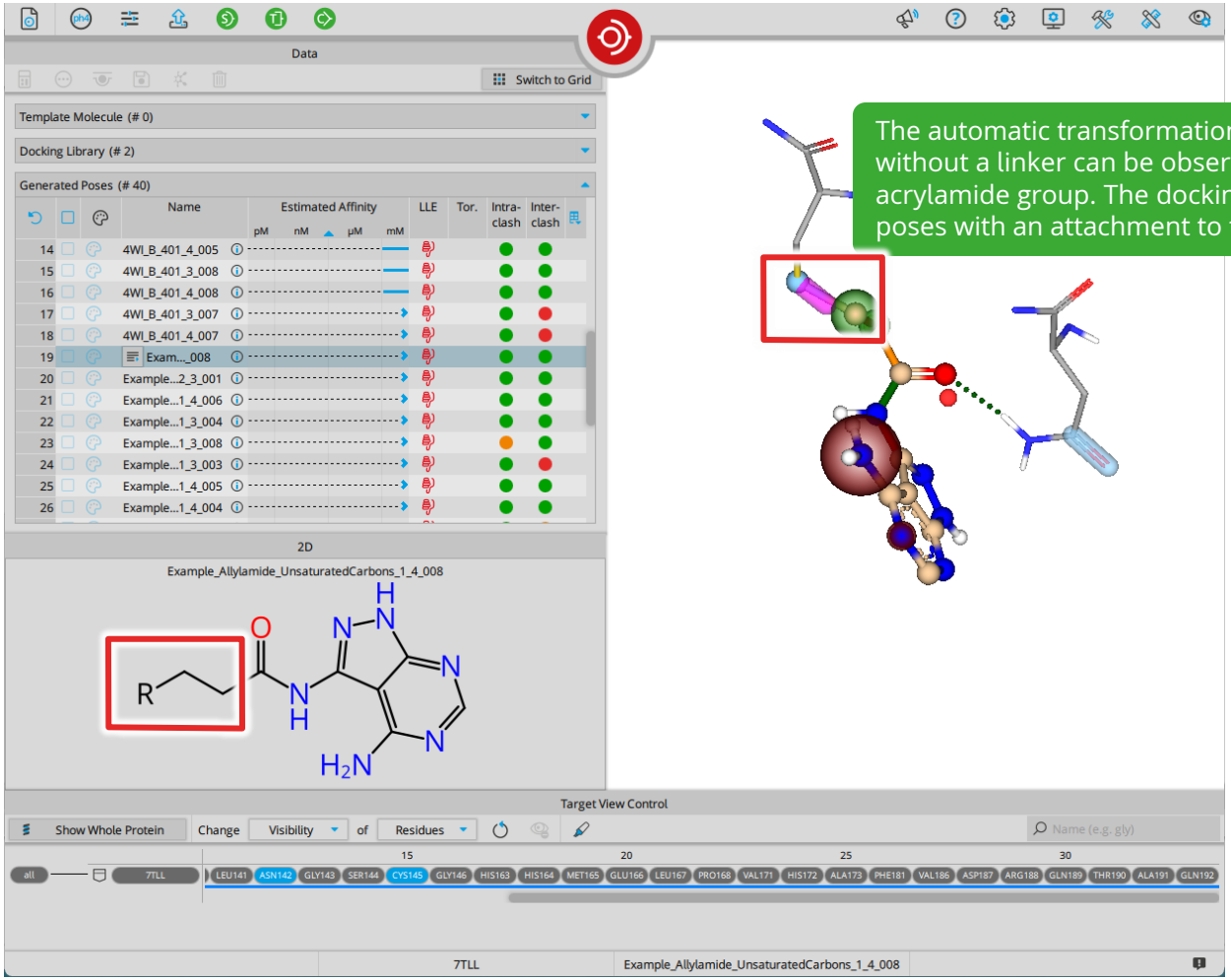


The pharmacophore and docking parameters can be adjusted as usual. For covalent docking, the parameter "Flexible Covalent Attachment" becomes relevant. This allows the user to choose whether the terminal bond of the residue involved in covalent attachment should be rotatable. By default, it is set to flexible.

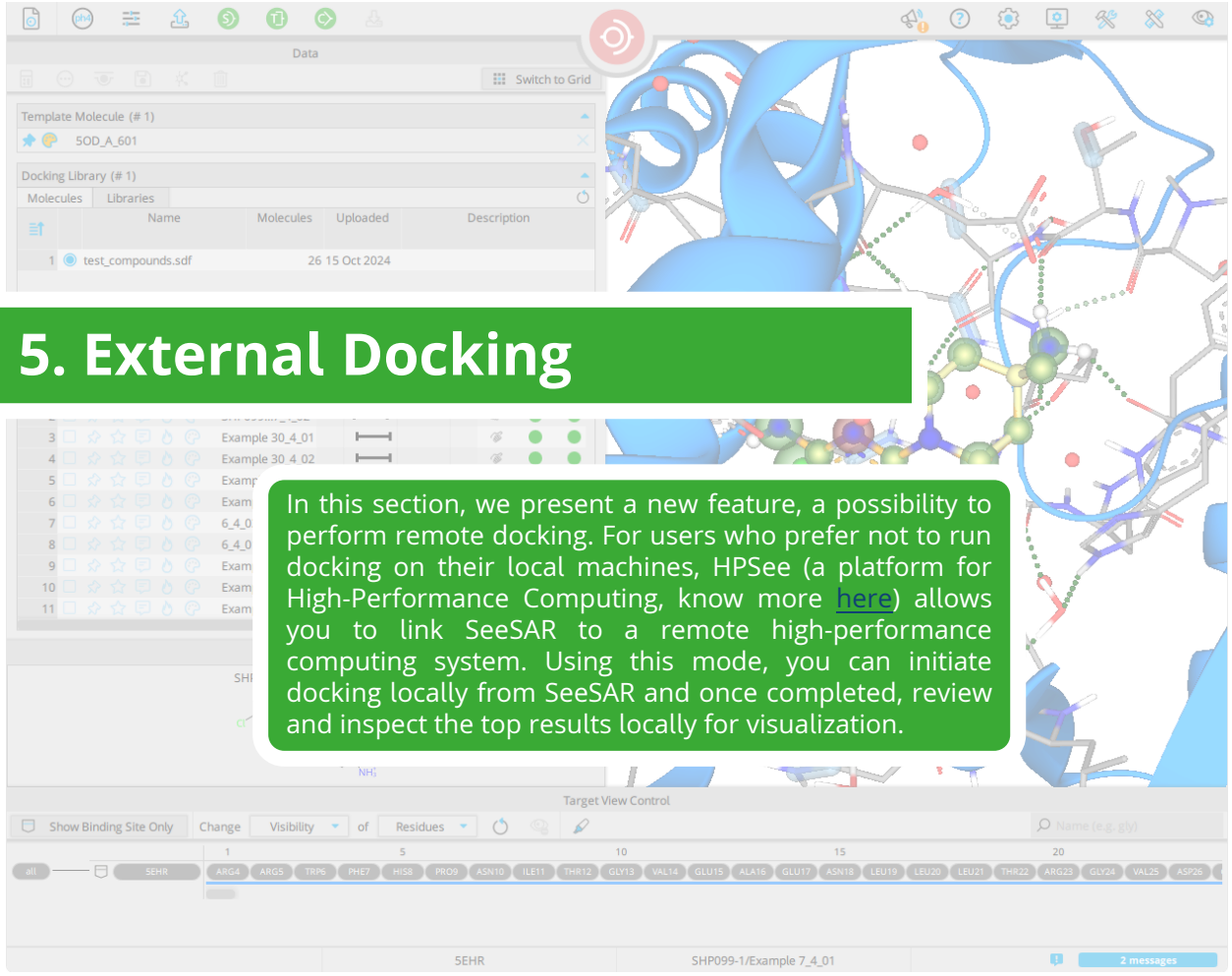
Once all the parameters are set, click the third green docking button for Covalent Docking to initiate the process.



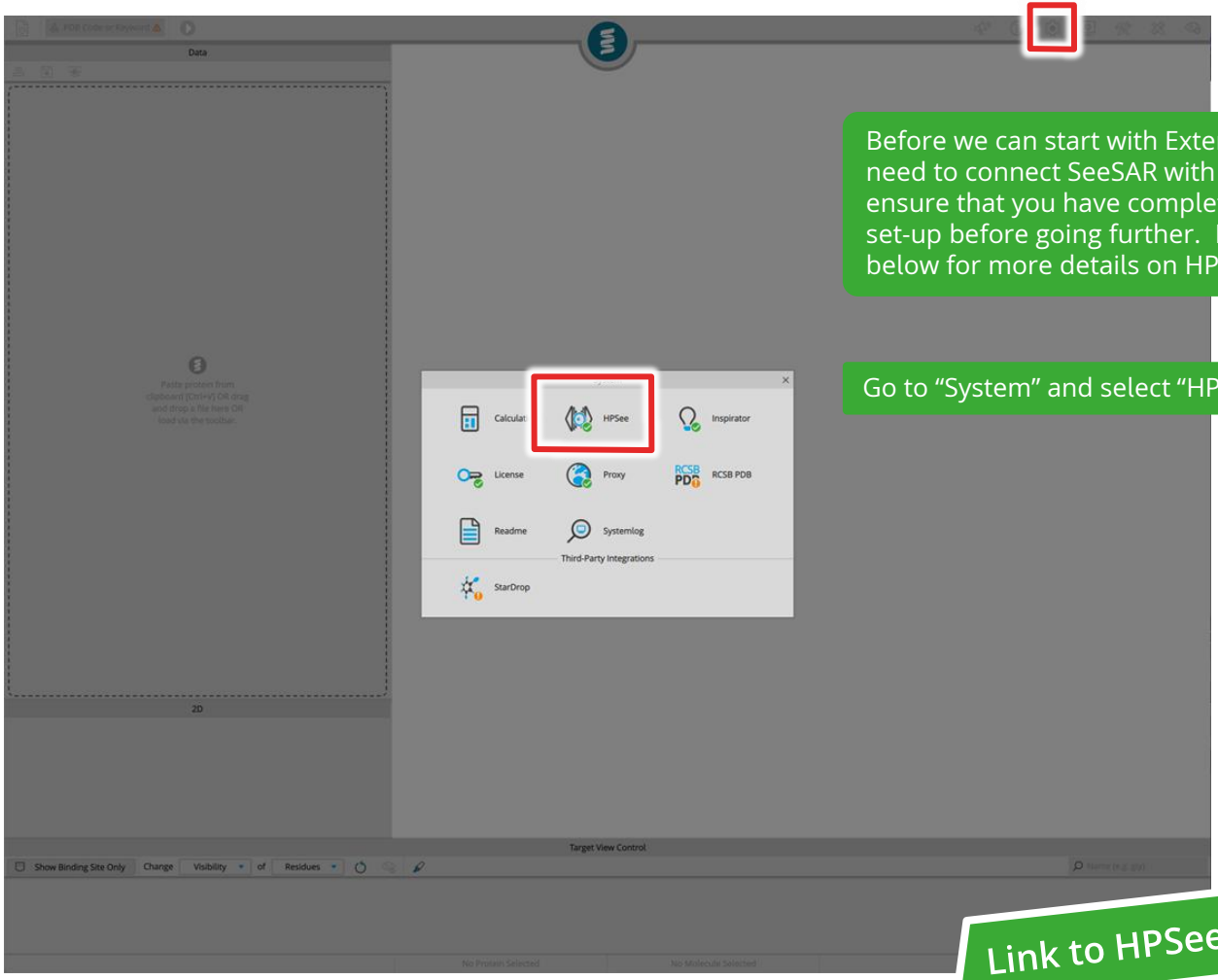
Your results will be displayed in the “Generated Poses” table.


Data
Switch to Grid
Template Molecule (# 0)
Docking Library (# 2)
Generated Poses (# 40)
Name
Estimated Affinity
pM nM µM mM
LLE
Tor.
Intra-clash
Inter-clash
14 4WI_B_401_4_005
15 4WI_B_401_3_008
16 4WI_B_401_4_008
17 4WI_B_401_3_007
18 4WI_B_401_4_007
19 Exam..._008
20 Example...2_3_001
21 Example...1_4_006
22 Example...1_3_004
23 Example...1_3_008
24 Example...1_3_003
25 Example...1_4_005
26 Example...1_4_004
2D
Example_Allylamide_UnsaturatedCarbons_1_4_008
R
O
N
H
N
N
N
H2N
The automatic transformation of the ligand without a linker can be observed for the acrylamide group. The docking has generated poses with an attachment to this linker.
Target View Control
Show Whole Protein
Change
Visibility
of
Residues
Name (e.g. gly)
15
20
25
30
all
7TLL
LEU141 ASN142 GLY143 SER144 CYS145 GLY146 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 VAL171 HIS172 ALA173 PHE181 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192
7TLL
Example_Allylamide_UnsaturatedCarbons_1_4_008

5. External Docking



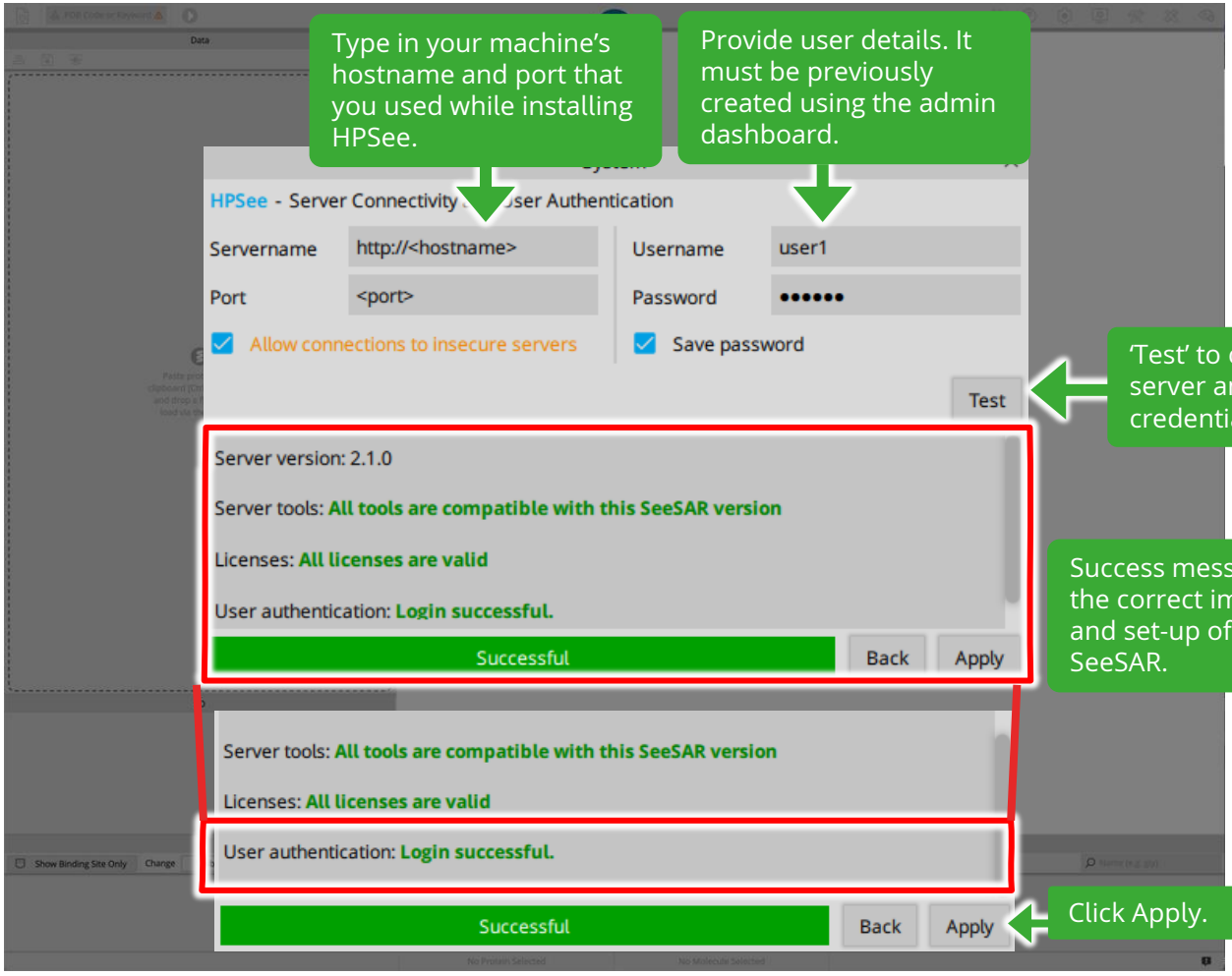
In this section, we present a new feature, a possibility to perform remote docking. For users who prefer not to run docking on their local machines, HPSee (a platform for High-Performance Computing, know more here) allows you to link SeeSAR to a remote high-performance computing system. Using this mode, you can initiate docking locally from SeeSAR and once completed, review and inspect the top results locally for visualization.

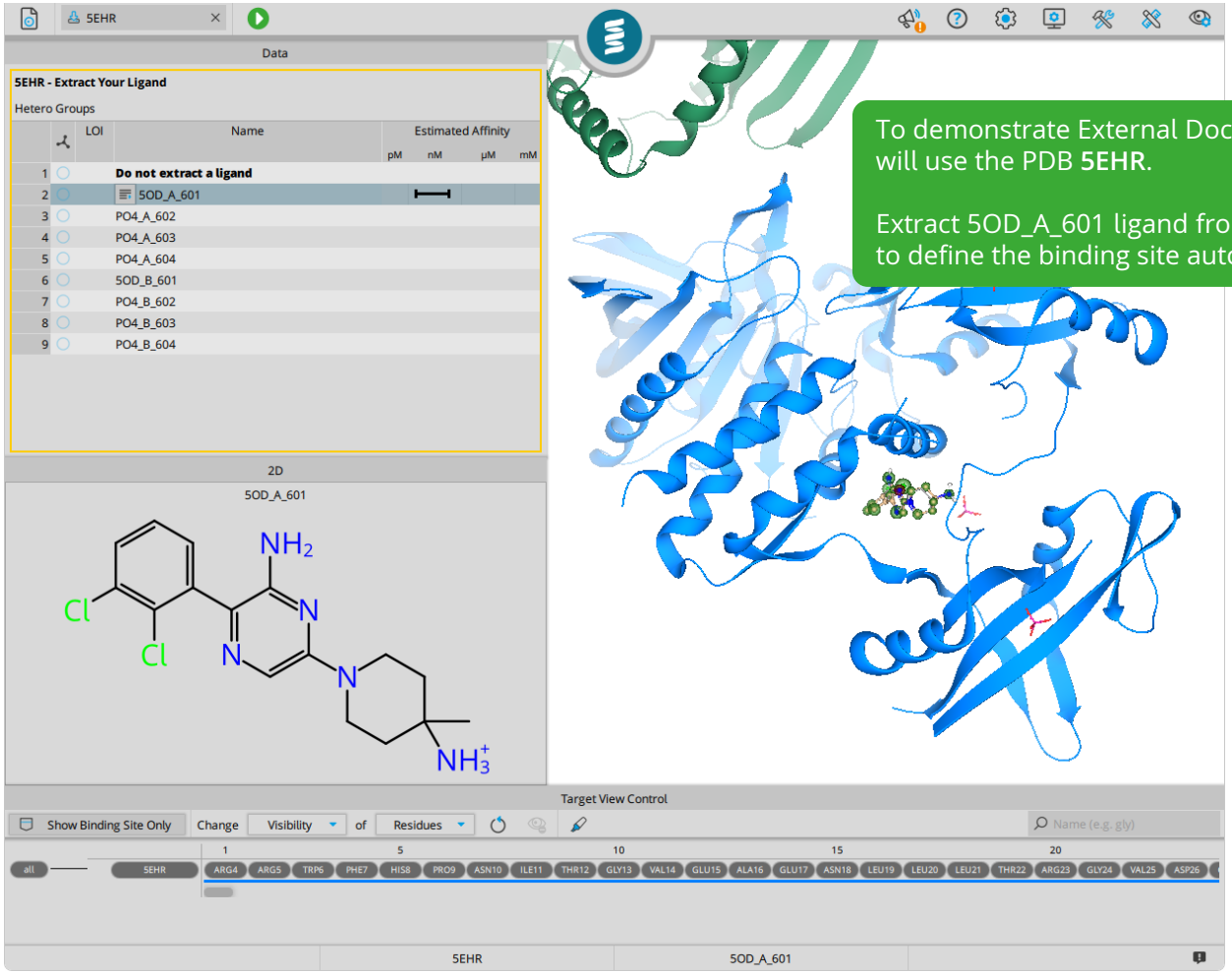


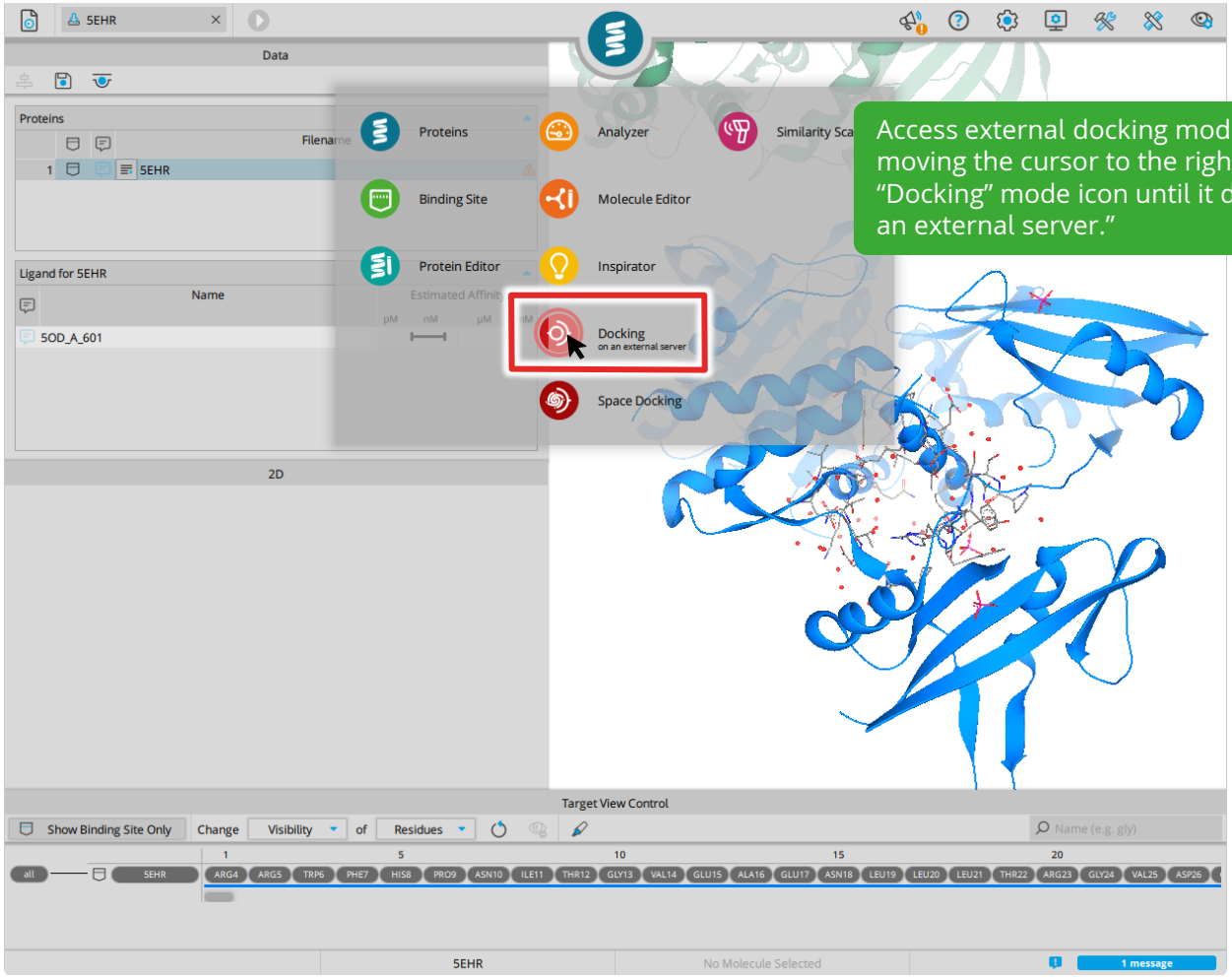
Before we can start with External Docking, we need to connect SeeSAR with HPSee. Please ensure that you have completed your HPSee set-up before going further. Refer to the guide below for more details on HPSee.

Go to “System” and select “HPSee”.

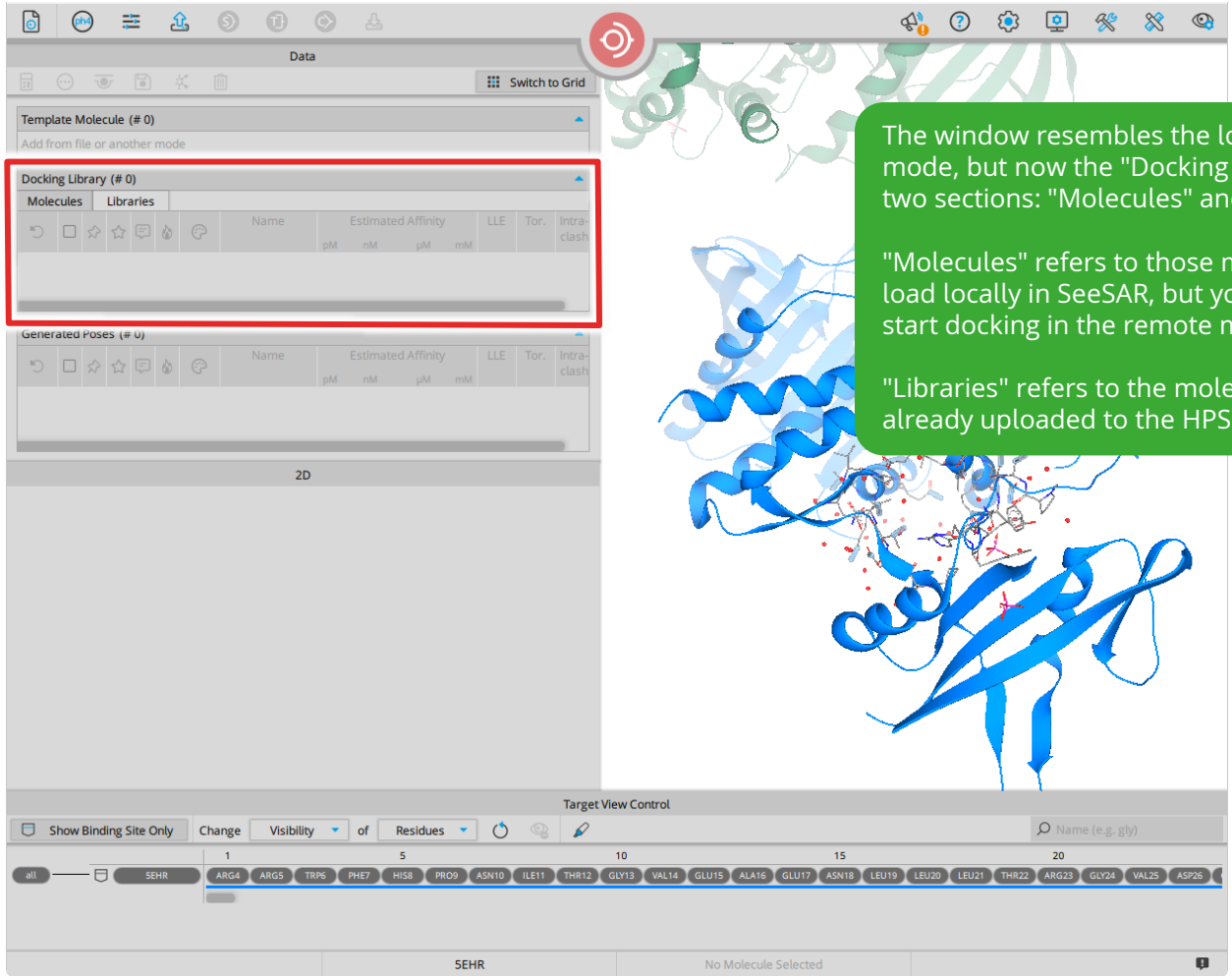
Link to HPSee guide


Type in your machine's hostname and port that you used while installing HPSee.
Provide user details. It must be previously created using the admin dashboard.
HPSee - Server Connectivity
User Authentication
Servername
http://<hostname>
Username
user1
Port
<port>
Password
Allow connections to insecure servers
Save password
Test
'Test' to check validity of server and login credentials.
Server version: 2.1.0
Server tools: All tools are compatible with this SeeSAR version
Licenses: All licenses are valid
User authentication: Login successful.
Successful
Back
Apply
Success message indicates the correct implementation and set-up of HPSee and SeeSAR.
Server tools: All tools are compatible with this SeeSAR version
Licenses: All licenses are valid
User authentication: Login successful.
Successful
Back
Apply
Click Apply.


5EHR
Data
5EHR - Extract Your Ligand
Hetero Groups
LOI
Name
Estimated Affinity
pM nM µM mM
1 Do not extract a ligand
2 5OD_A_601
3 PO4_A_602
4 PO4_A_603
5 PO4_A_604
6 5OD_B_601
7 PO4_B_602
8 PO4_B_603
9 PO4_B_604
2D
5OD_A_601
NH2
Cl
Cl
N
N
N
NH3+
To demonstrate External Docking, we will use the PDB 5EHR.
Extract 5OD_A_601 ligand from Chain A to define the binding site automatically.
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
Name (e.g. gly)
all
5EHR
ARG4 ARG5 TRP6 PHE7 HIS8 PRO9 ASN10 ILE11 THR12 GLY13 VAL14 GLU15 ALA16 GLU17 ASN18 LEU19 LEU20 LEU21 THR22 ARG23 GLY24 VAL25 ASP26
5EHR
5OD_A_601



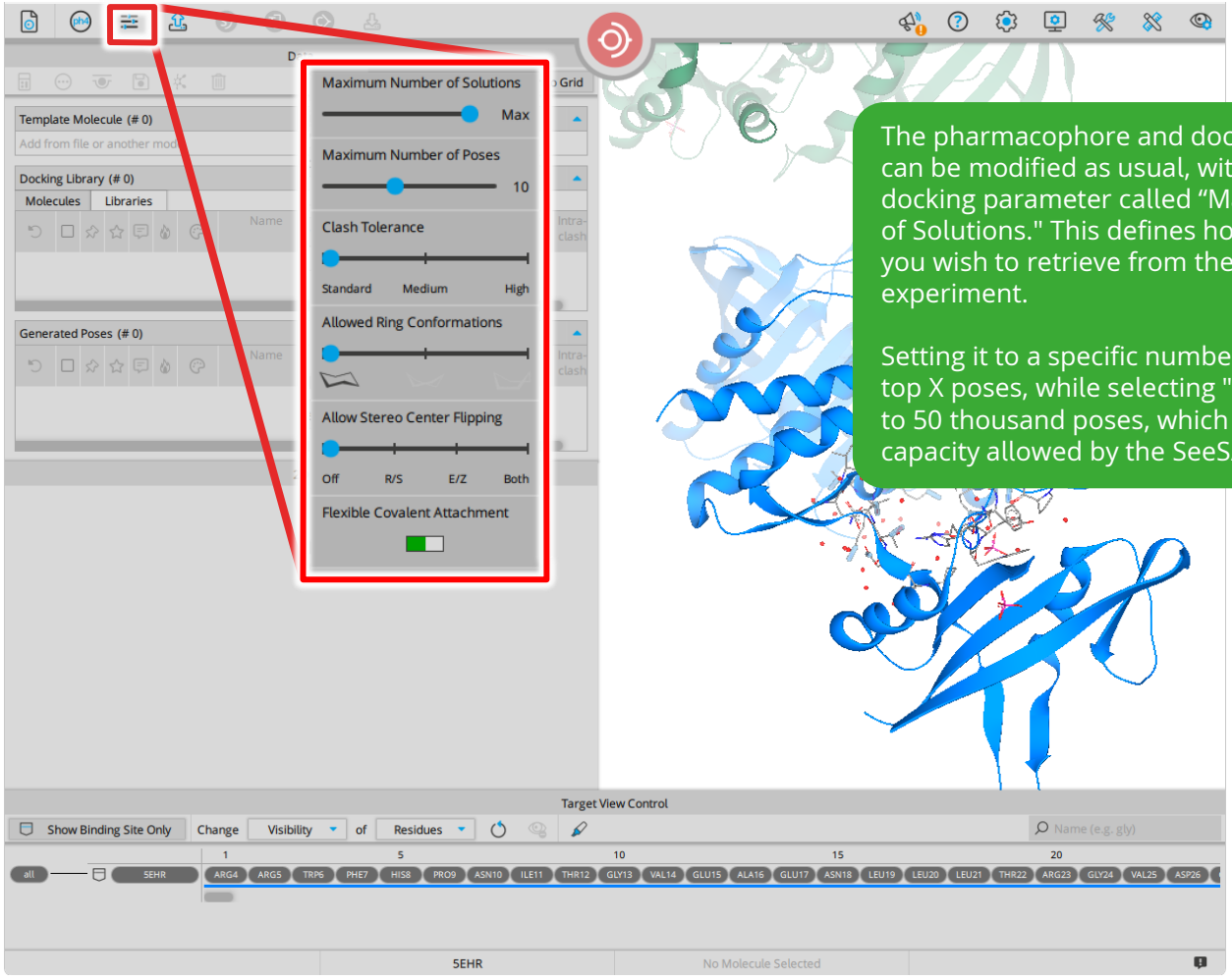
Access external docking mode by moving the cursor to the right on the "Docking" mode icon until it displays "on an external server."



The window resembles the local docking mode, but now the "Docking library" has two sections: "Molecules" and "Libraries."

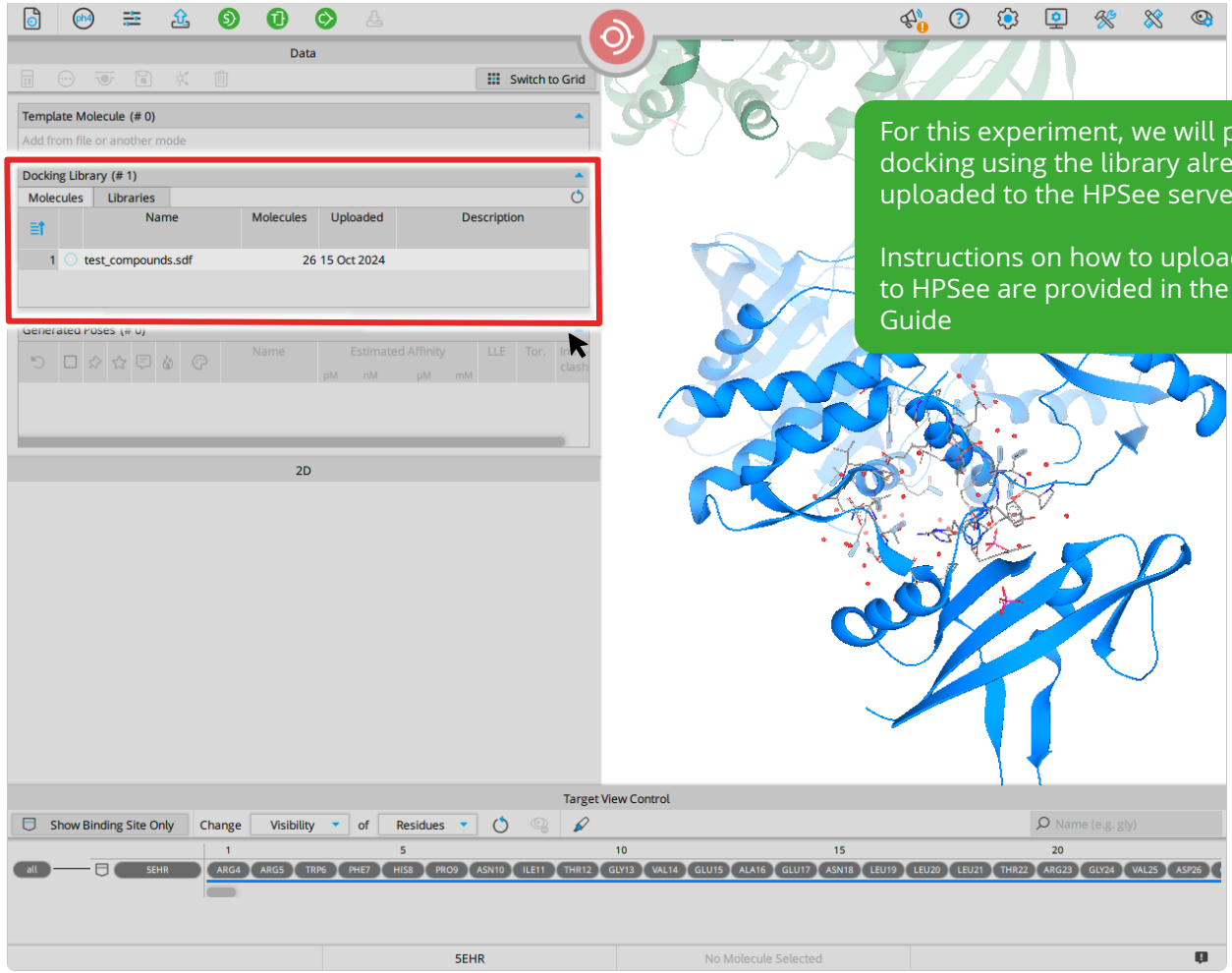
"Molecules" refers to those molecules you load locally in SeeSAR, but you intend to start docking in the remote machine.

"Libraries" refers to the molecule library already uploaded to the HPSee server.



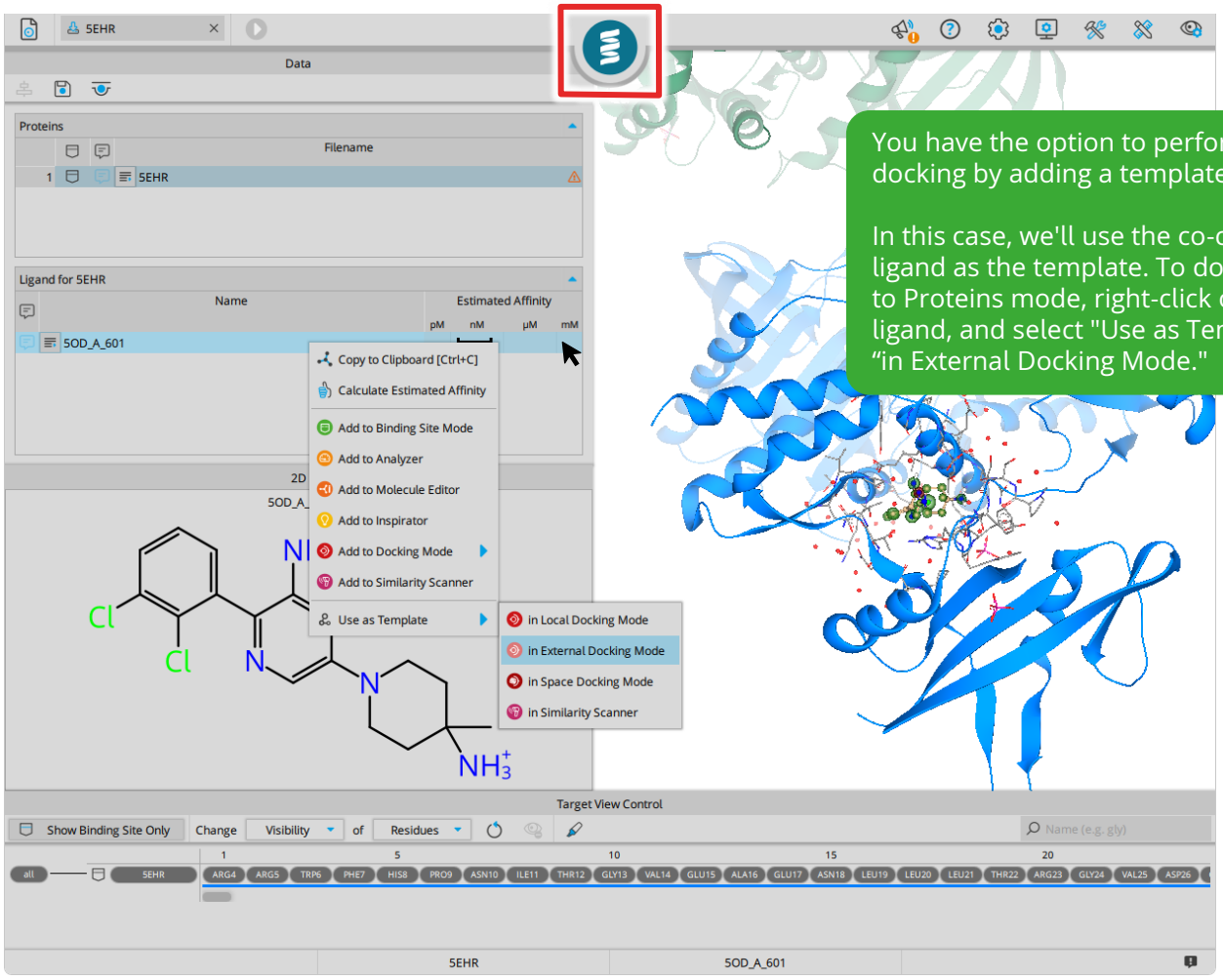
The pharmacophore and docking parameters can be modified as usual, with an additional docking parameter called “Maximum Number of Solutions." This defines how many top poses you wish to retrieve from the docking experiment.

Setting it to a specific number X will return the top X poses, while selecting "Max" retrieves up to 50 thousand poses, which is the maximum capacity allowed by the SeeSAR table.



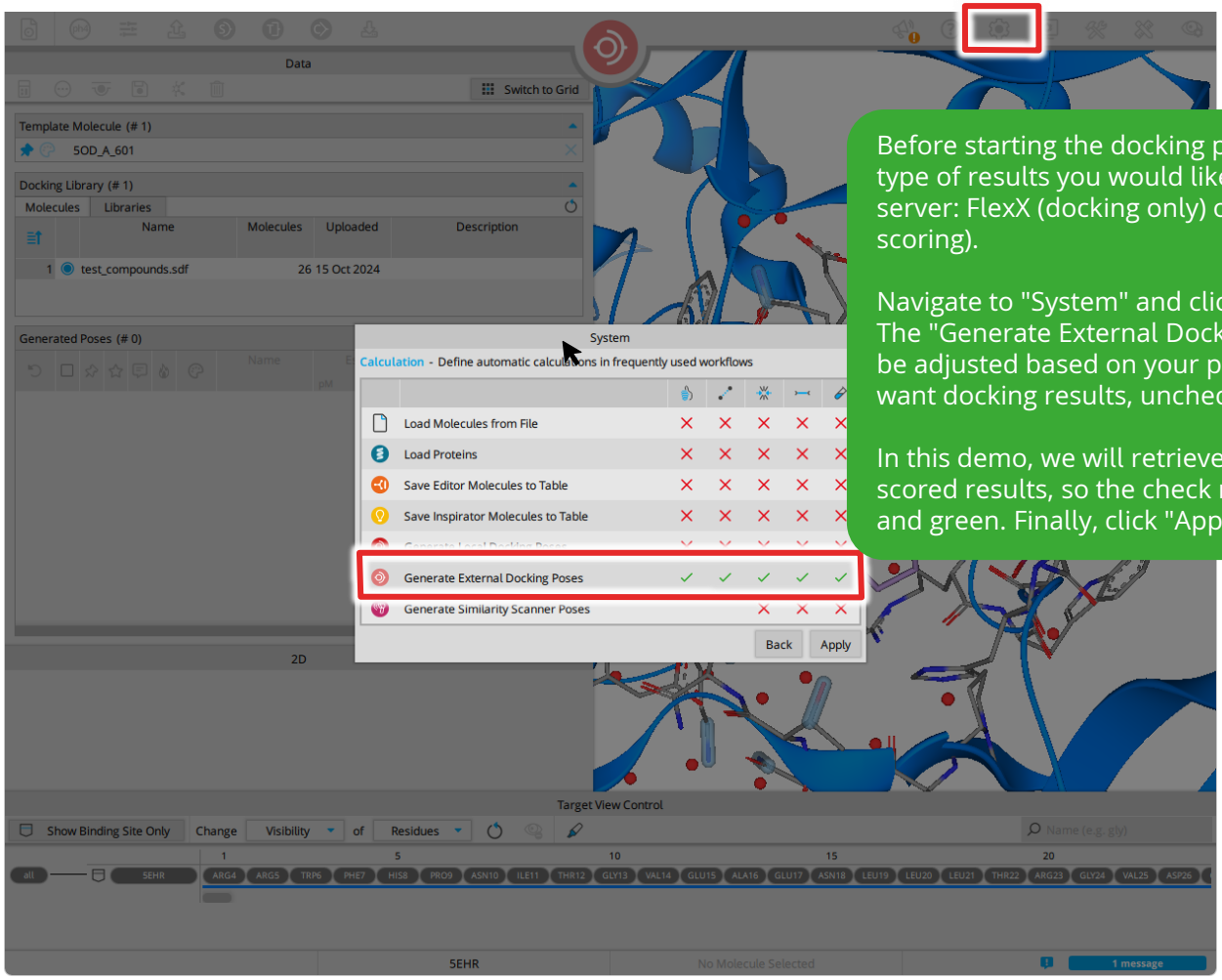
For this experiment, we will perform docking using the library already uploaded to the HPSee server.

Instructions on how to upload a library to HPSee are provided in the HPSee Guide



You have the option to perform template docking by adding a template molecule.

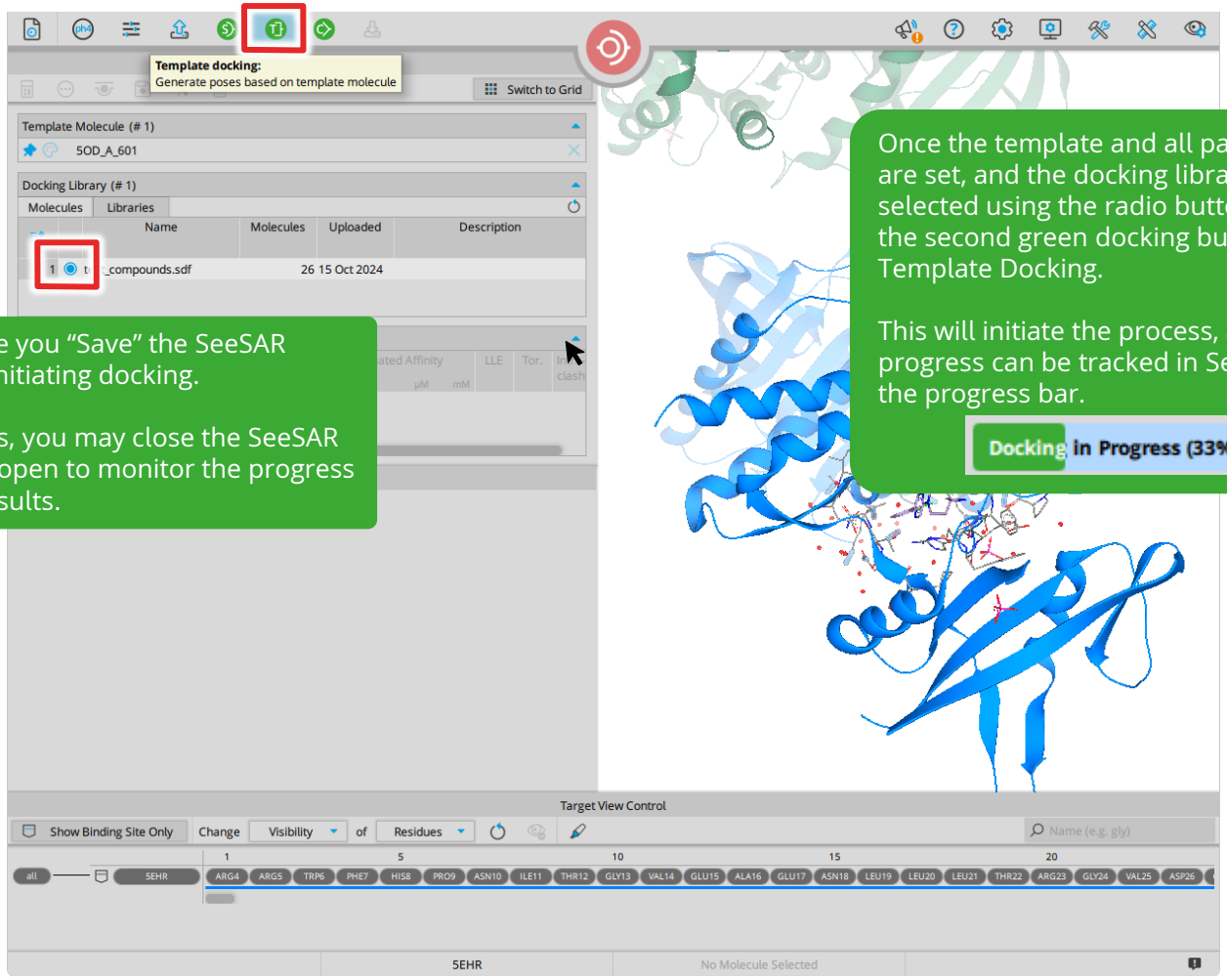
In this case, we'll use the co-crystallized ligand as the template. To do this, return to Proteins mode, right-click on the ligand, and select "Use as Template" and “in External Docking Mode."



Before starting the docking process, decide what type of results you would like to retrieve from the server: FlexX (docking only) or HYDE (docking and scoring).

Navigate to "System" and click on "Calculation." The "Generate External Docking Poses" option can be adjusted based on your preference. If you only want docking results, uncheck the boxes.

In this demo, we will retrieve both docked and scored results, so the check marks are enabled and green. Finally, click "Apply."



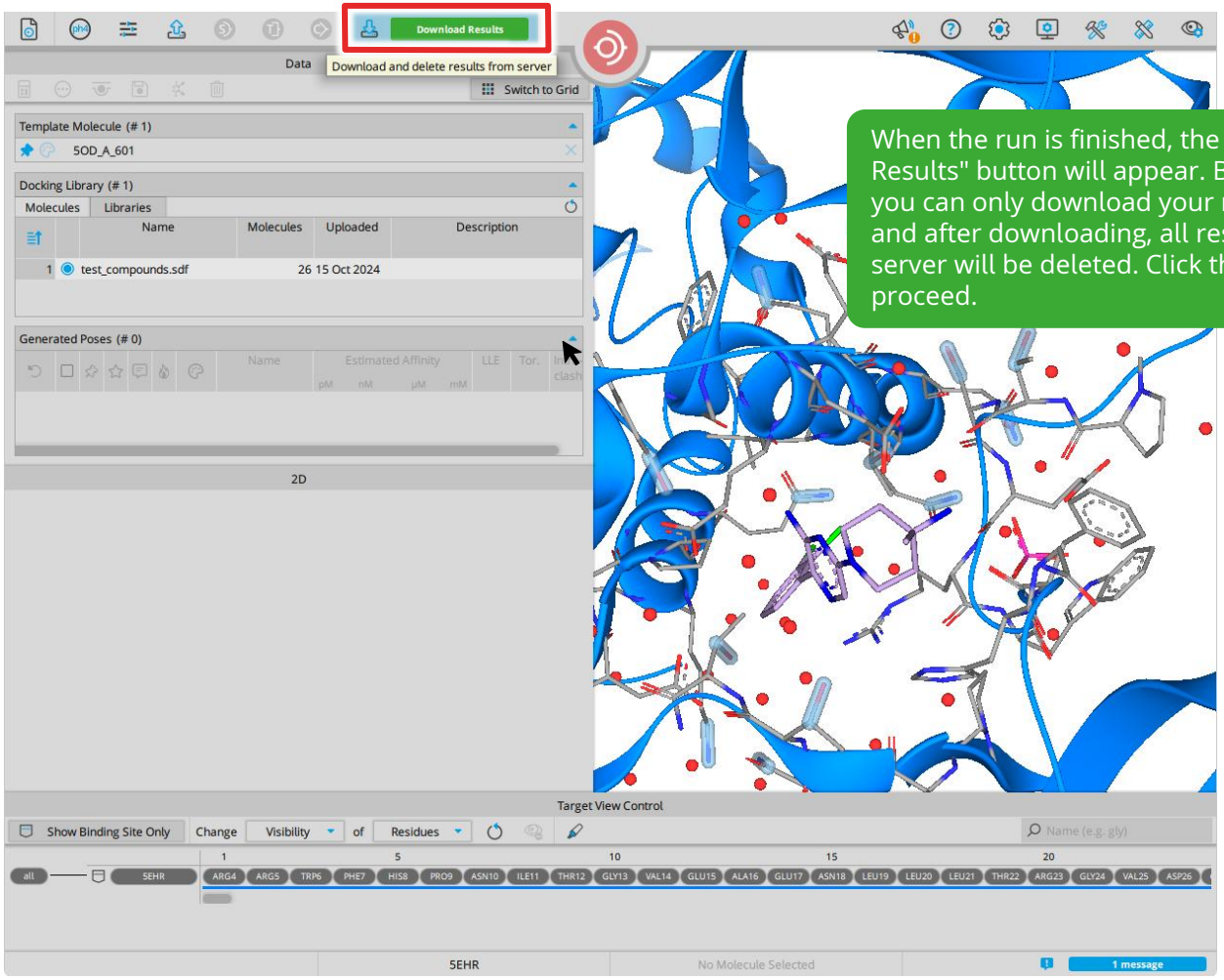
At this stage, ensure you “Save” the SeeSAR project file before initiating docking.

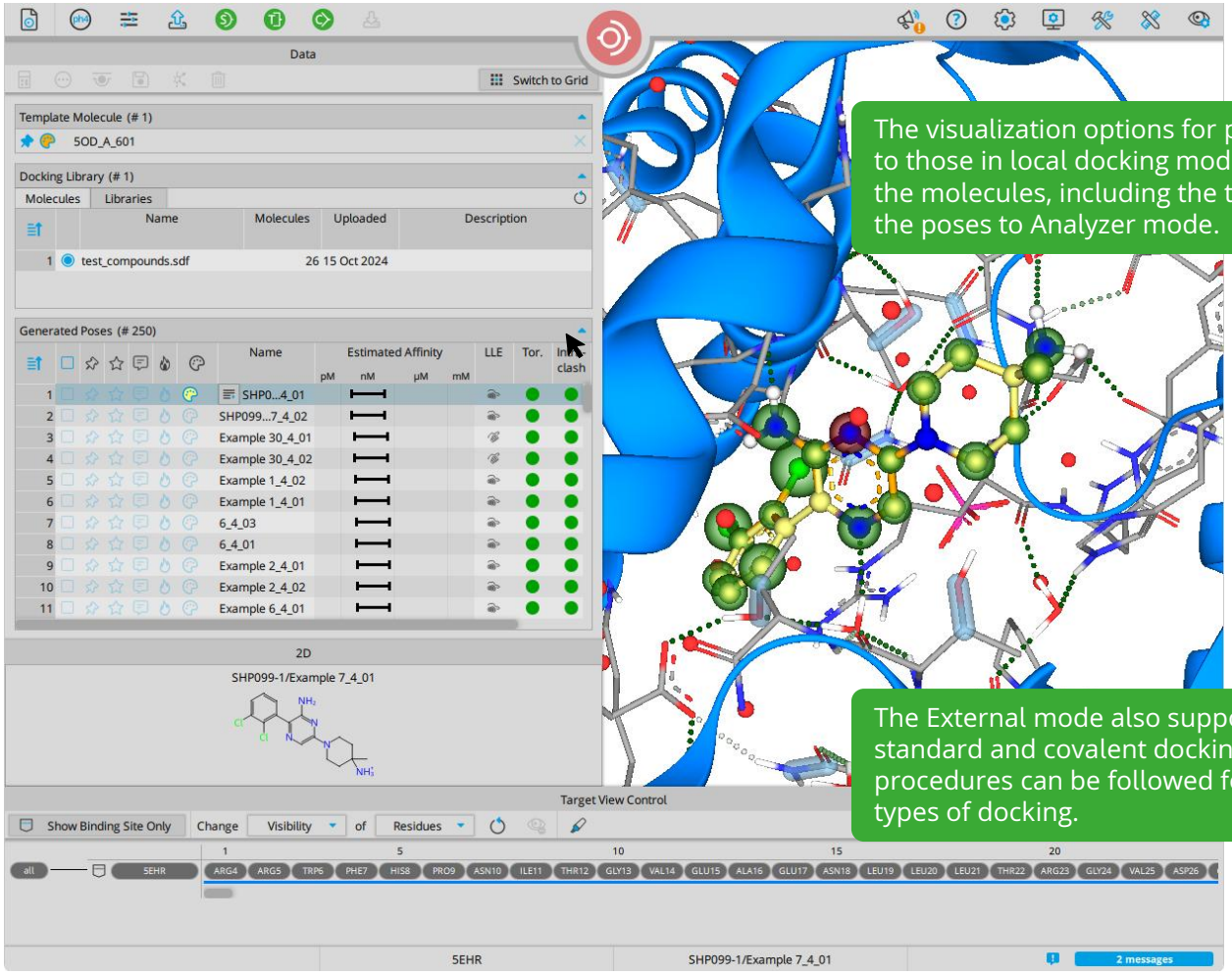
Once the run begins, you may close the SeeSAR project and later reopen to monitor the progress or download the results.

Once the template and all parameters are set, and the docking library is selected using the radio button, click the second green docking button: Template Docking.

This will initiate the process, and the progress can be tracked in SeeSAR via the progress bar.

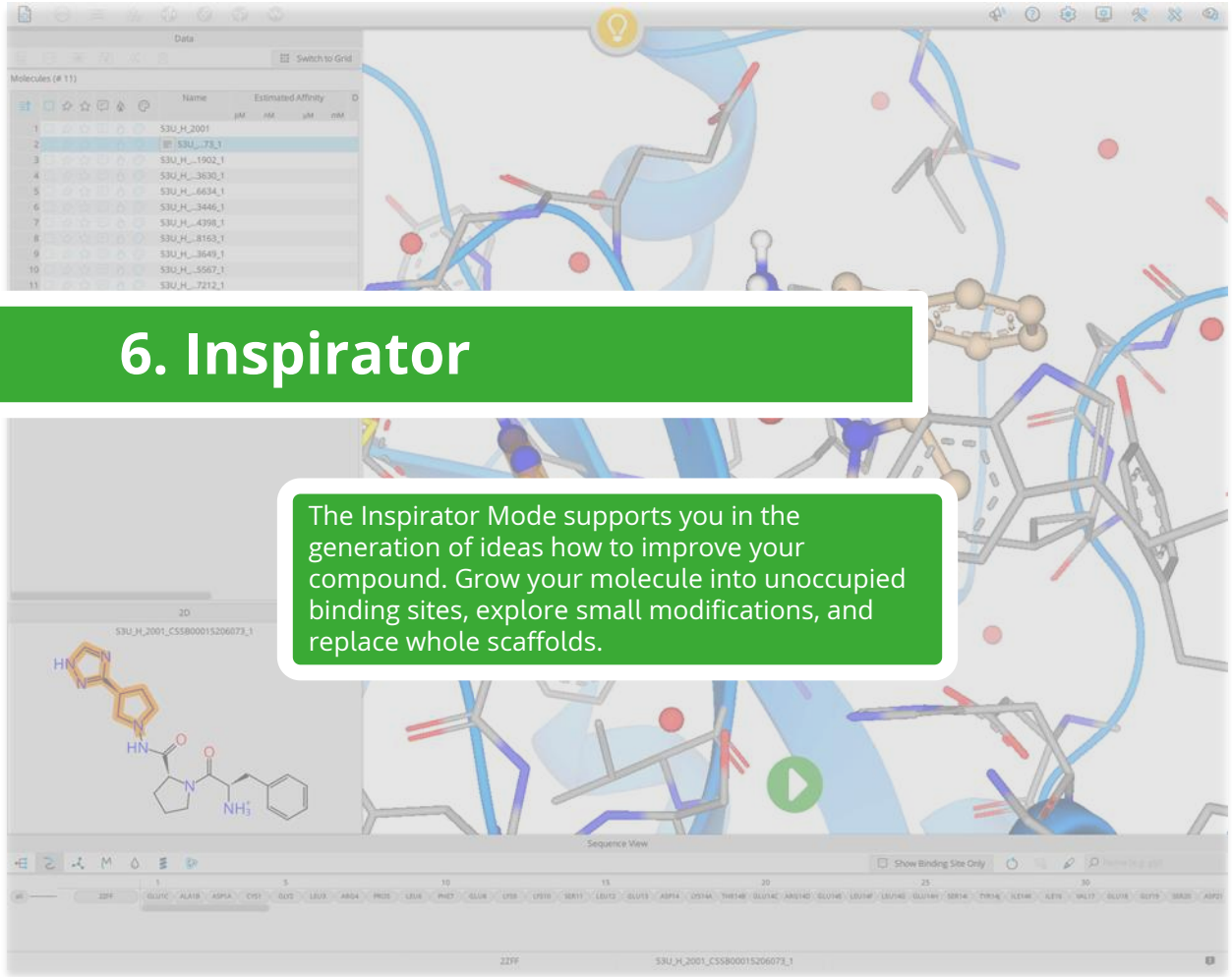
Docking in Progress (33%)


Download Results
Download and delete results from server
Data
Switch to Grid
Template Molecule (# 1)
5OD_A_601
Docking Library (# 1)
Molecules
Libraries
Name
Molecules
Uploaded
Description
1
test_compounds.sdf
26 15 Oct 2024
Generated Poses (# 0)
Name
Estimated Affinity
LLE
Tor.
2D
When the run is finished, the "Download Results" button will appear. Be aware that you can only download your results once, and after downloading, all results on the server will be deleted. Click the button to proceed.
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
Name (e.g. gly)
all
5EHR
ARG4
ARG5
TRP6
PHE7
HIS8
PRO9
ASN10
ILE11
THR12
GLY13
VAL14
GLU15
ALA16
GLU17
ASN18
LEU19
LEU20
LEU21
THR22
ARG23
GLY24
VAL25
ASP26
5EHR
No Molecule Selected
1 message



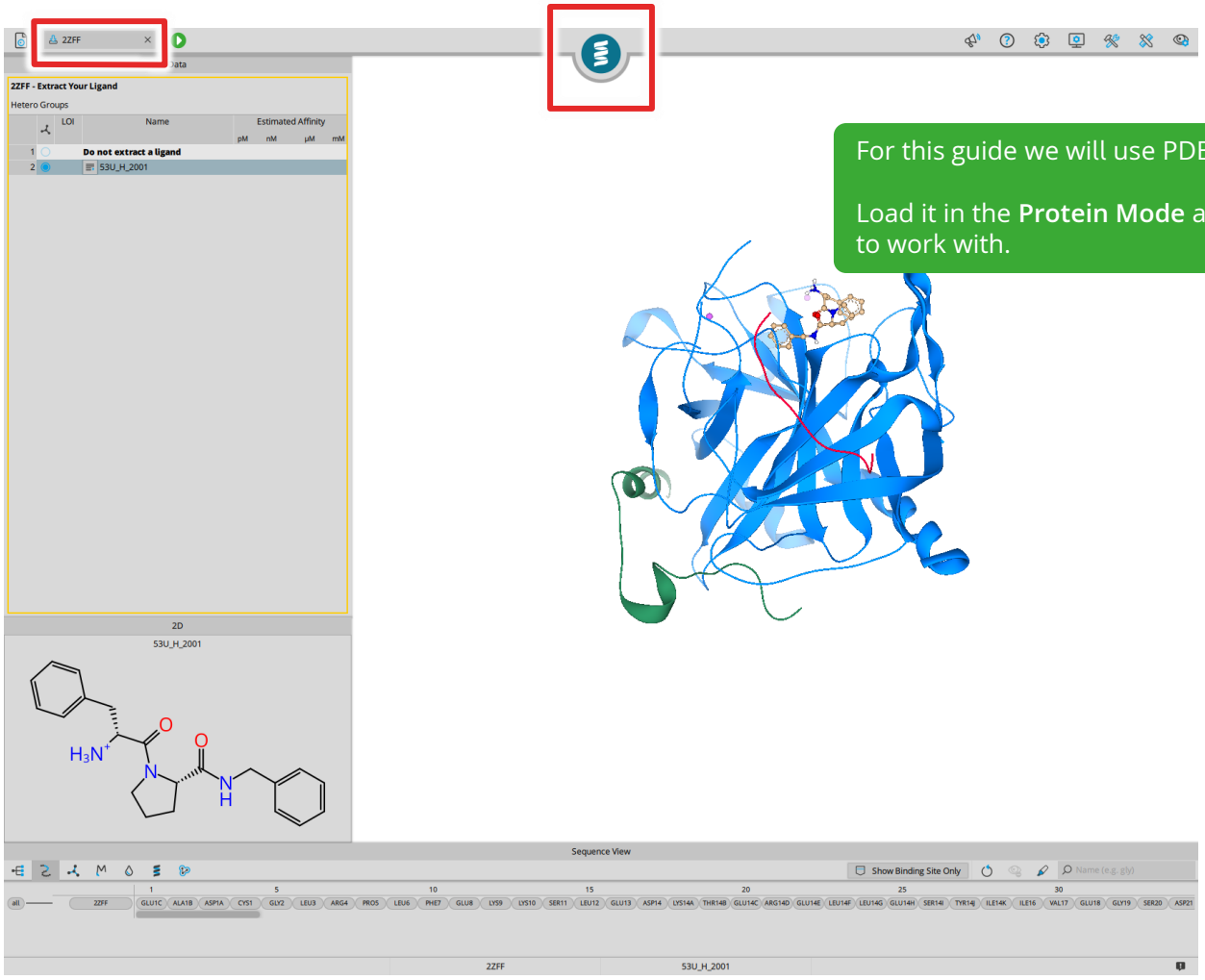
The visualization options for poses are similar to those in local docking mode. You can color the molecules, including the template, or move the poses to Analyzer mode.

The External mode also supports standard and covalent docking. Similar procedures can be followed for these types of docking.



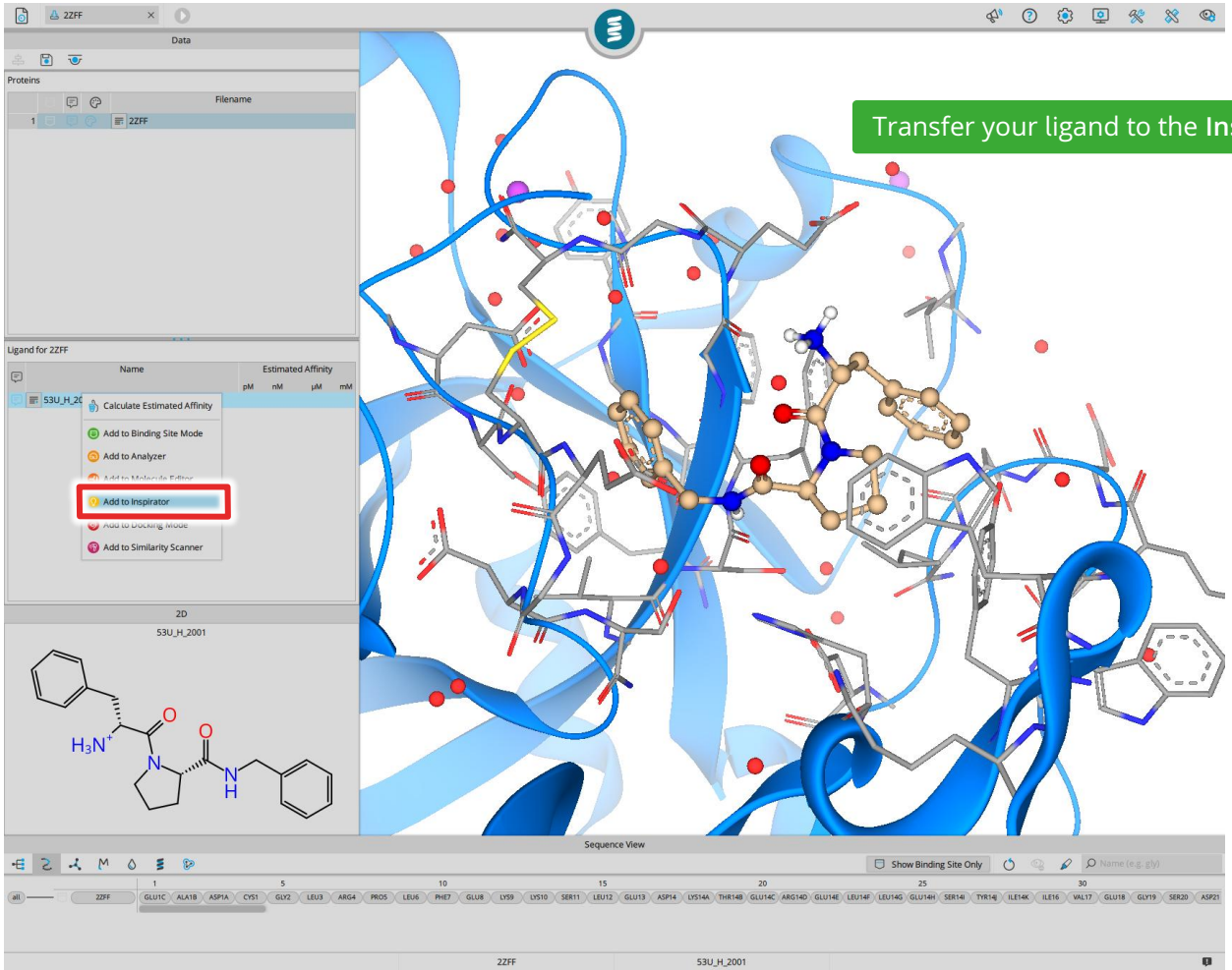
6. Inspirator

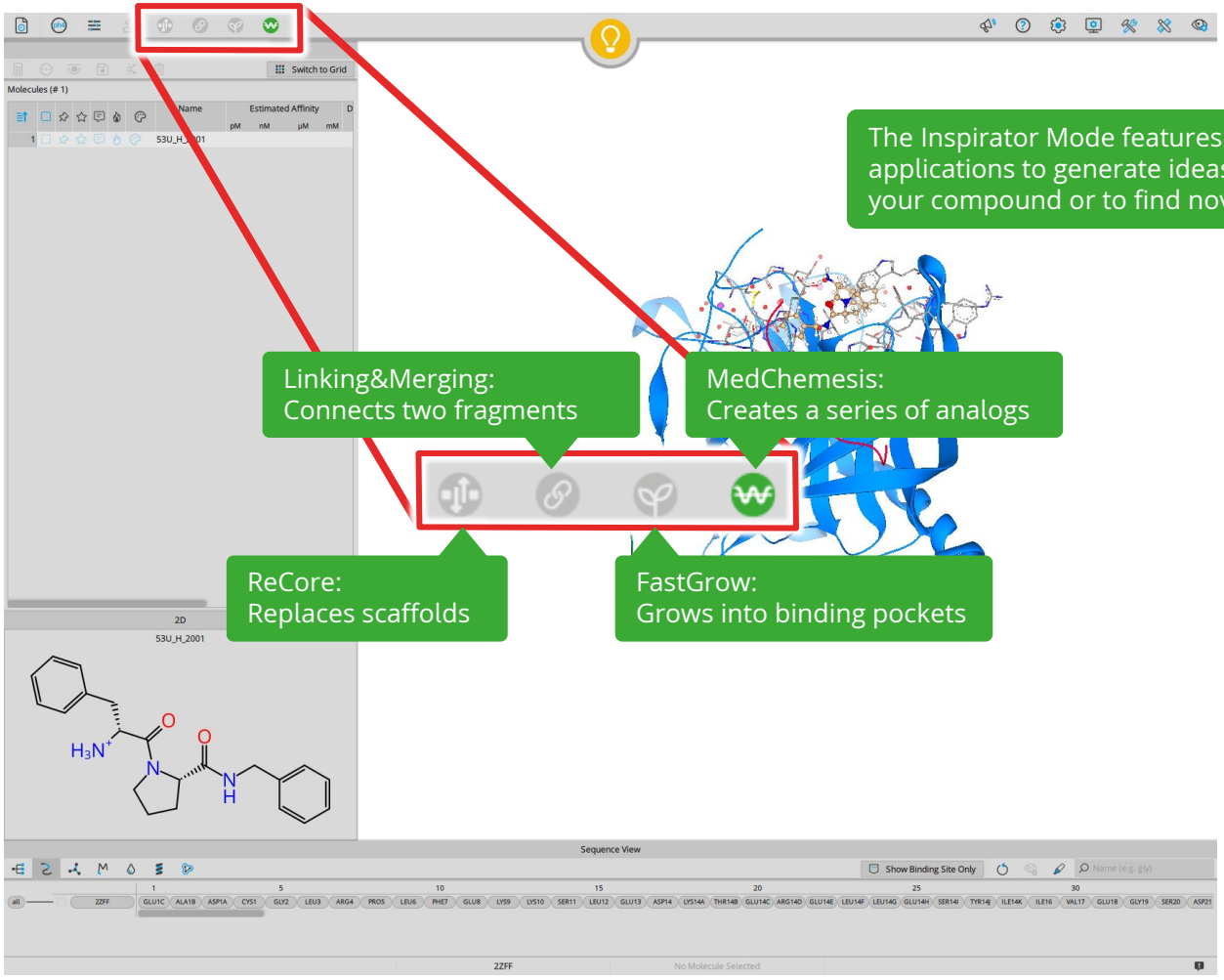
The Inspirator Mode supports you in the generation of ideas how to improve your compound. Grow your molecule into unoccupied binding sites, explore small modifications, and replace whole scaffolds.

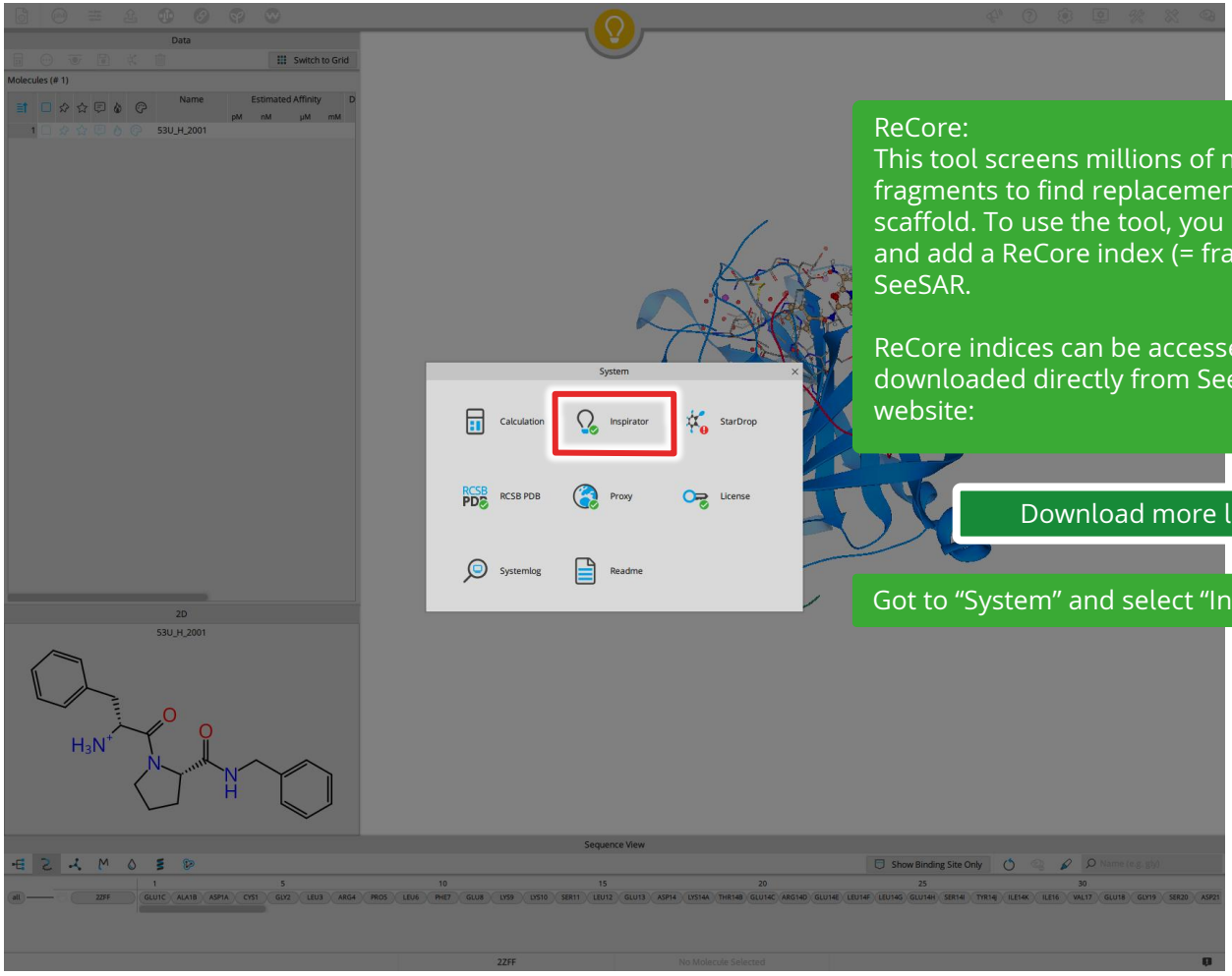


For this guide we will use PDB **2ZFF** as example.

Load it in the **Protein Mode** and select a ligand to work with.


2ZFF
Data
Proteins
Filename
1
2ZFF
Ligand for 2ZFF
Name
Estimated Affinity
pM
nM
µM
mM
53U_H_2001
Calculate Estimated Affinity
Add to Binding Site Mode
Add to Analyzer
Add to Inspirator
Add to Similarity Scanner
2D
53U_H_2001
Transfer your ligand to the **Inspirator Mode**.
Sequence View
Show Binding Site Only
2ZFF
53U_H_2001


The Inspirator Mode features several tools and applications to generate ideas how to improve your compound or to find novel scaffolds.
Linking&Merging:
Connects two fragments
MedChemesis:
Creates a series of analogs
ReCore:
Replaces scaffolds
FastGrow:
Grows into binding pockets
Switch to Grid
Molecules (# 1)
Name
Estimated Affinity
2D
53U_H_2001
Sequence View
Show Binding Site Only
2ZFF
No Molecule Selected

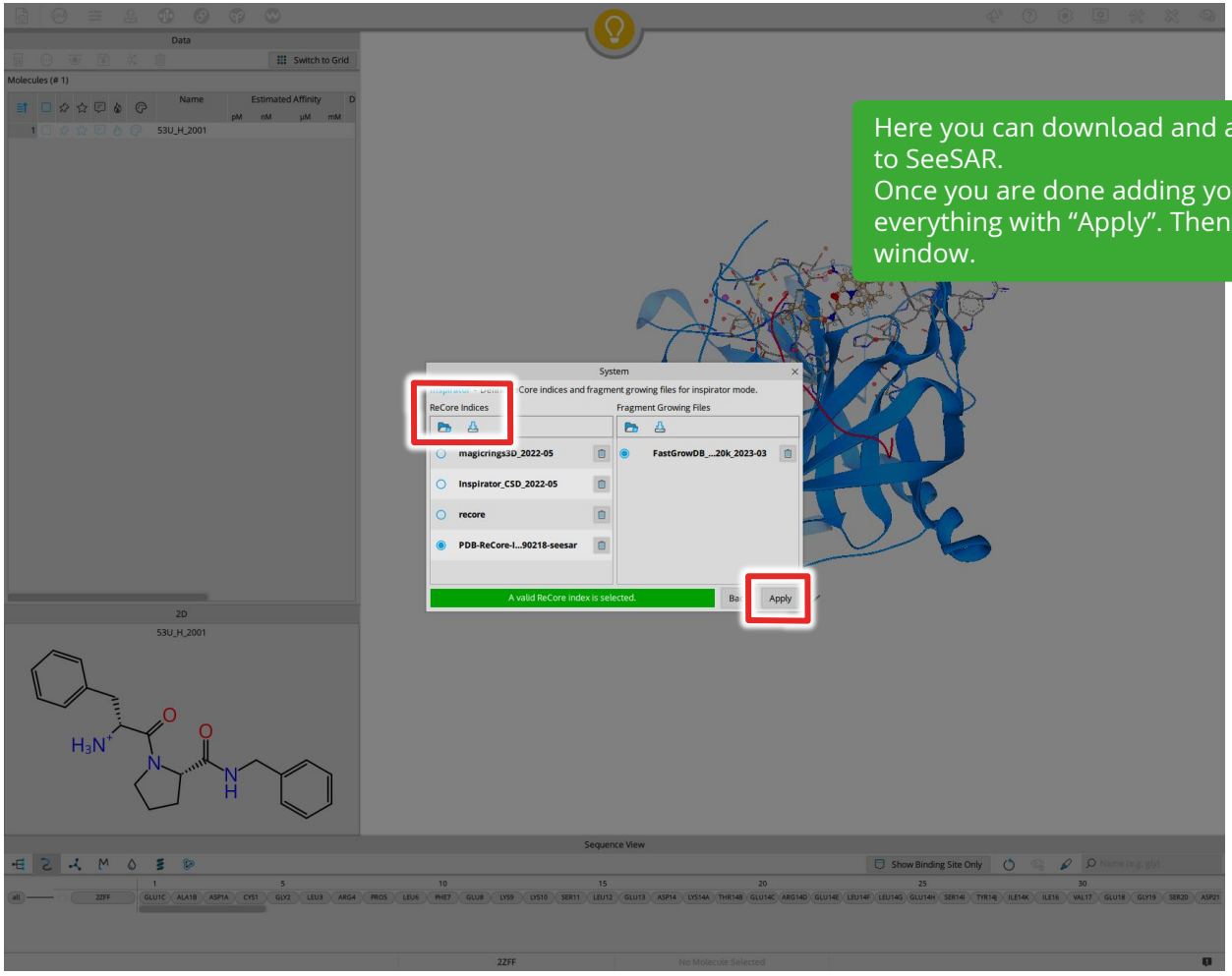


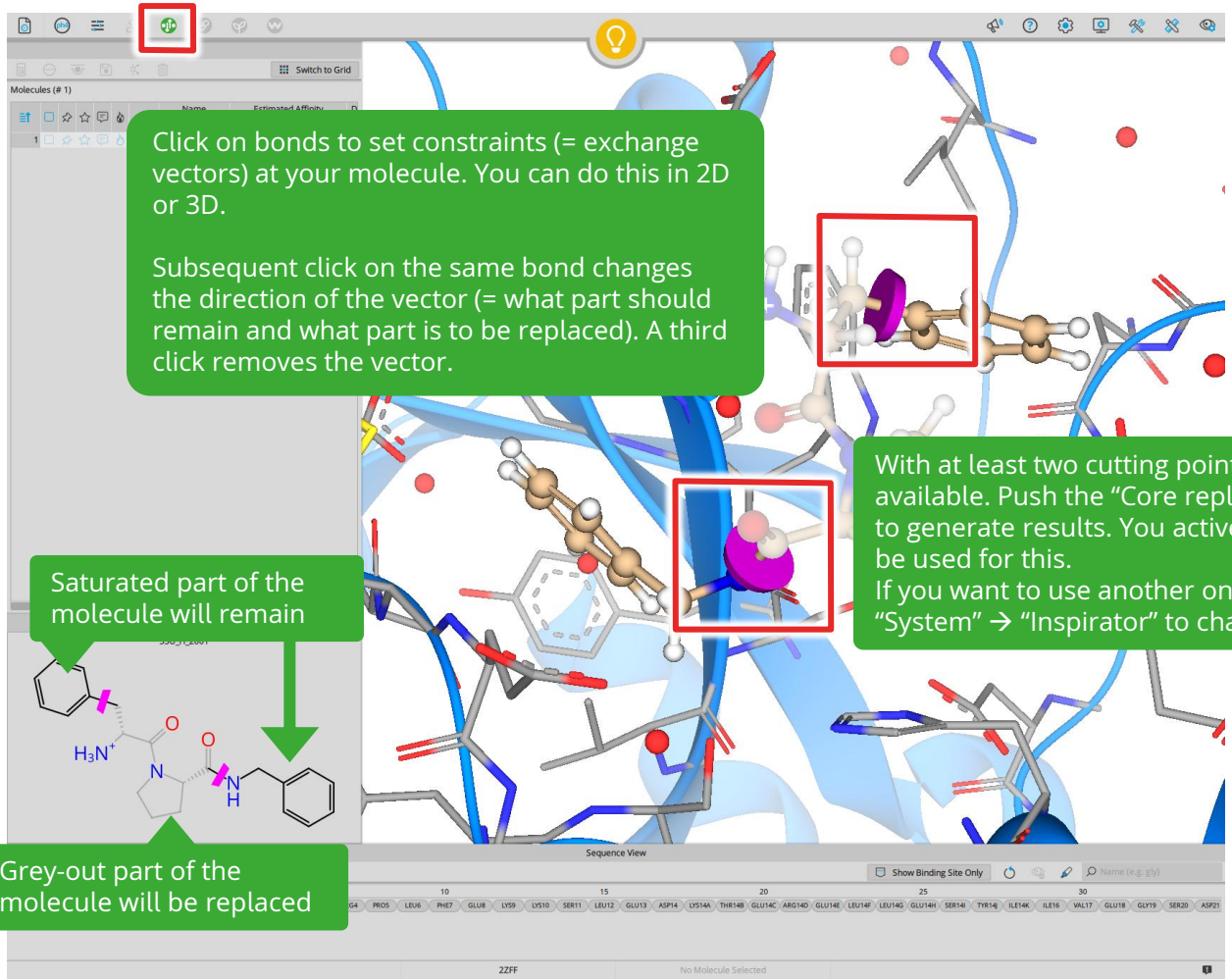
ReCore:
This tool screens millions of molecular fragments to find replacements for a 3D scaffold. To use the tool, you need to download and add a ReCore index (= fragment library) to SeeSAR.

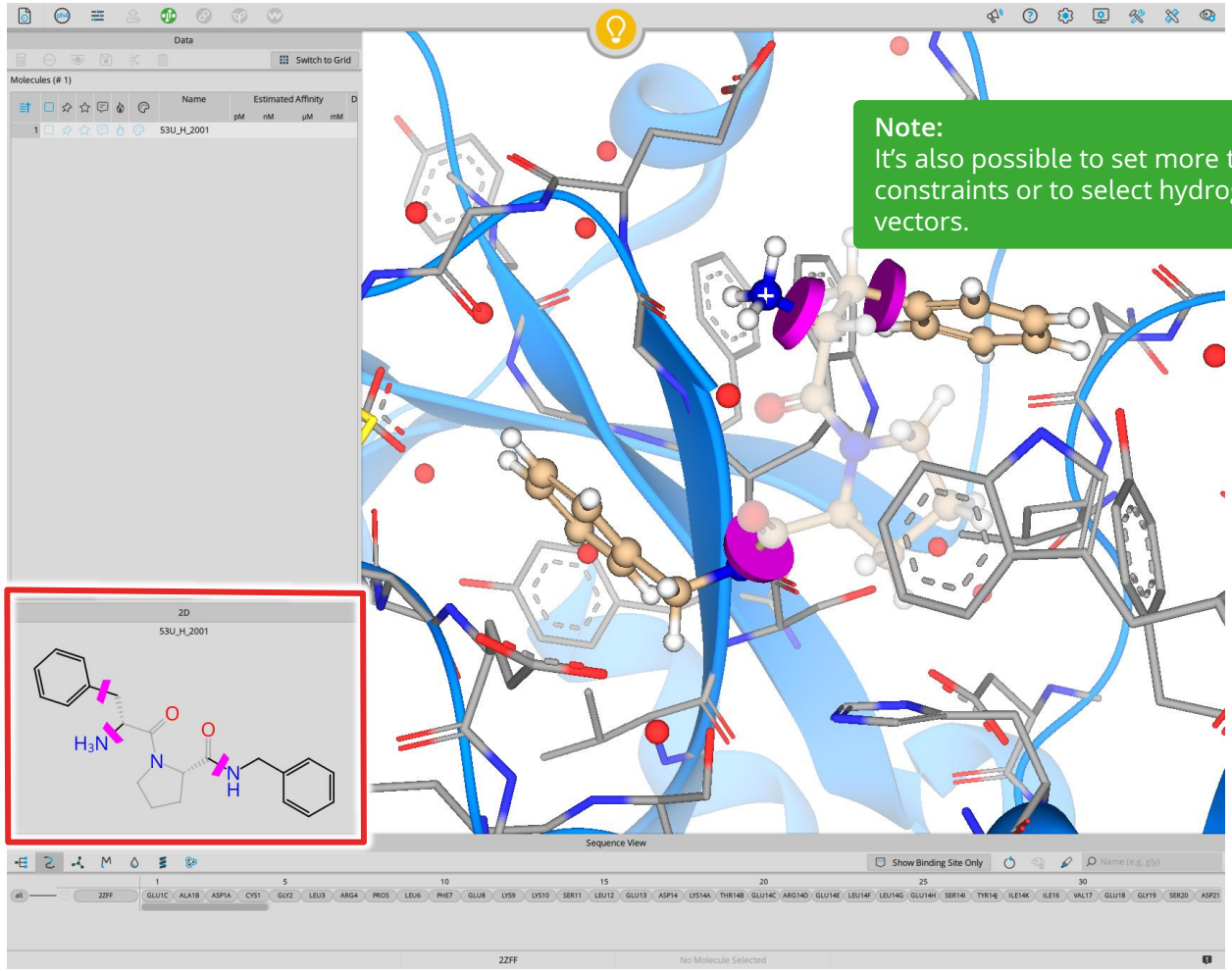
ReCore indices can be accessed and downloaded directly from SeeSAR or from our website:

Download more libraries

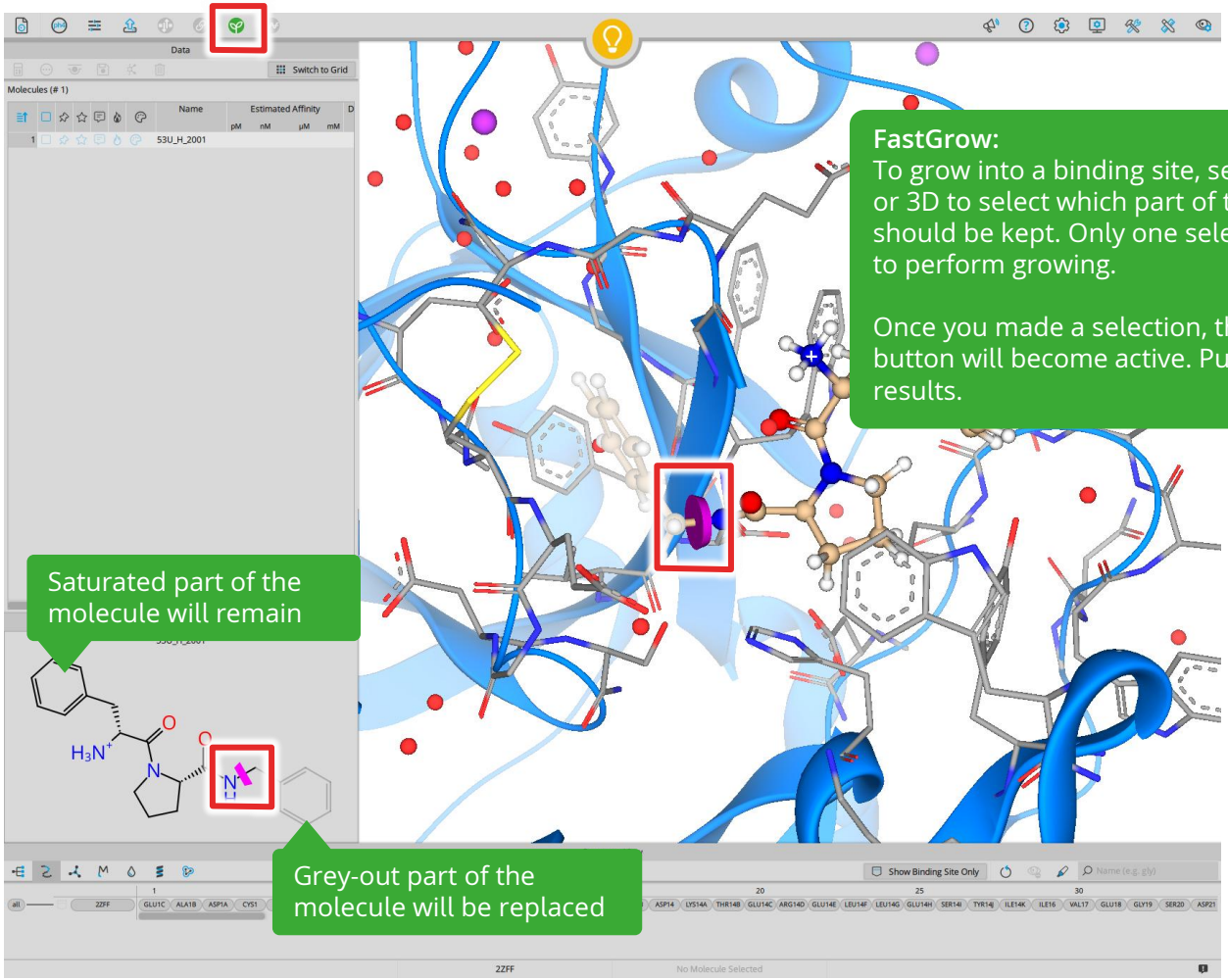
Got to “System” and select “Inspirator”.


Here you can download and add ReCore indices to SeeSAR.
Once you are done adding your indices, confirm everything with “Apply”. Then you can close the window.
System
Core indices and fragment growing files for inspirator mode.
ReCore Indices
Fragment Growing Files
magicrings3D_2022-05
Inspirator_CSD_2022-05
recore
PDB-ReCore-I...90218-seesar
FastGrowDB_...20k_2023-03
A valid ReCore index is selected.
Apply
Data
Switch to Grid
Molecules (# 1)
Name
Estimated Affinity
53U_H_2001
2D
Sequence View
Show Binding Site Only
2ZFF
No Molecule Selected


Click on bonds to set constraints (= exchange vectors) at your molecule. You can do this in 2D or 3D.
Subsequent click on the same bond changes the direction of the vector (= what part should remain and what part is to be replaced). A third click removes the vector.
With at least two cutting points ReCore becomes available. Push the “Core replacement” button to generate results. You active ReCore index will be used for this.
If you want to use another one, go back to “System” → “Inspirator” to change the index.
Saturated part of the molecule will remain
Grey-out part of the molecule will be replaced
Switch to Grid
Molecules (# 1)
Sequence View
Show Binding Site Only
2ZFF
No Molecule Selected

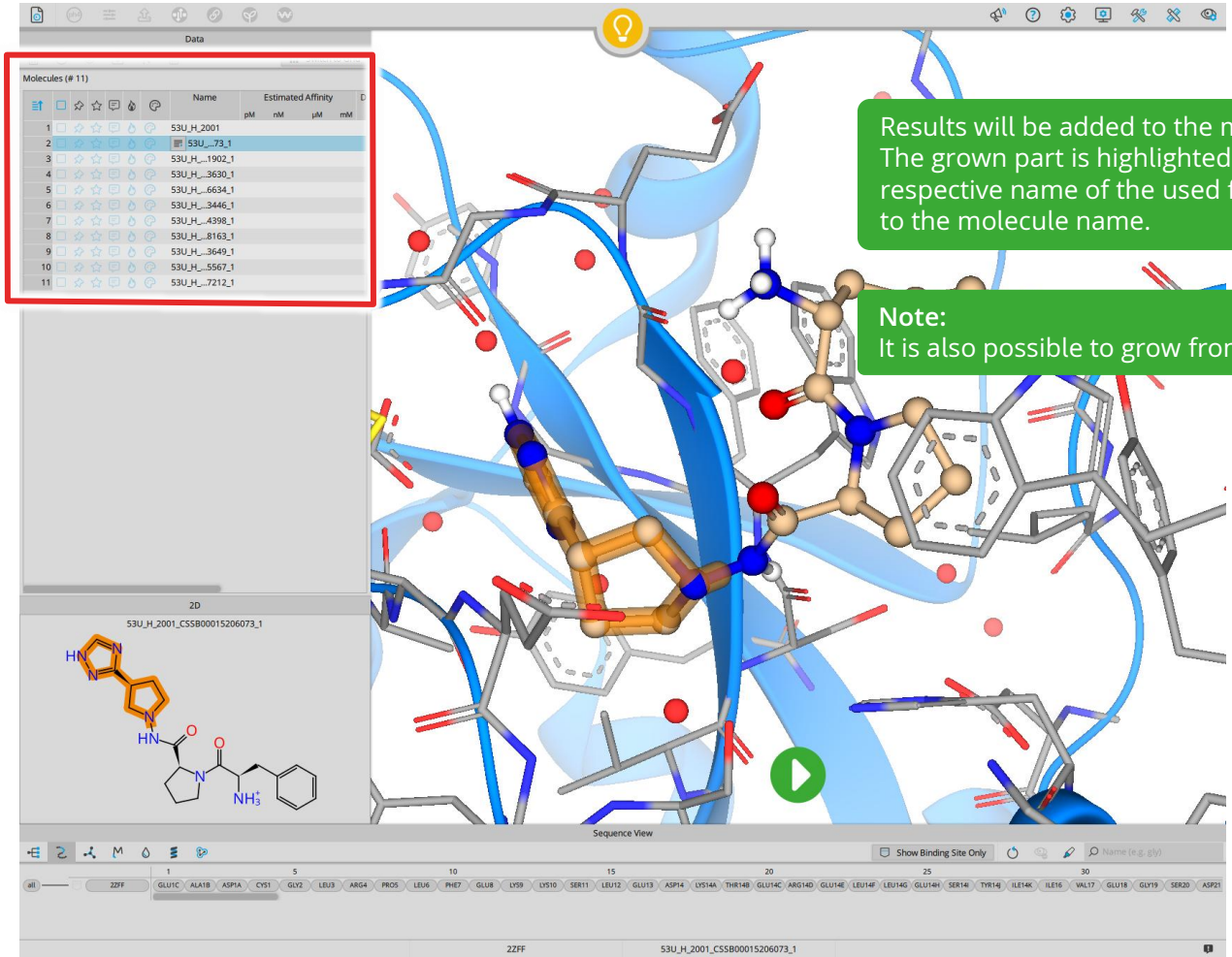


Note:
It's also possible to set more than two constraints or to select hydrogen bonds as vectors.



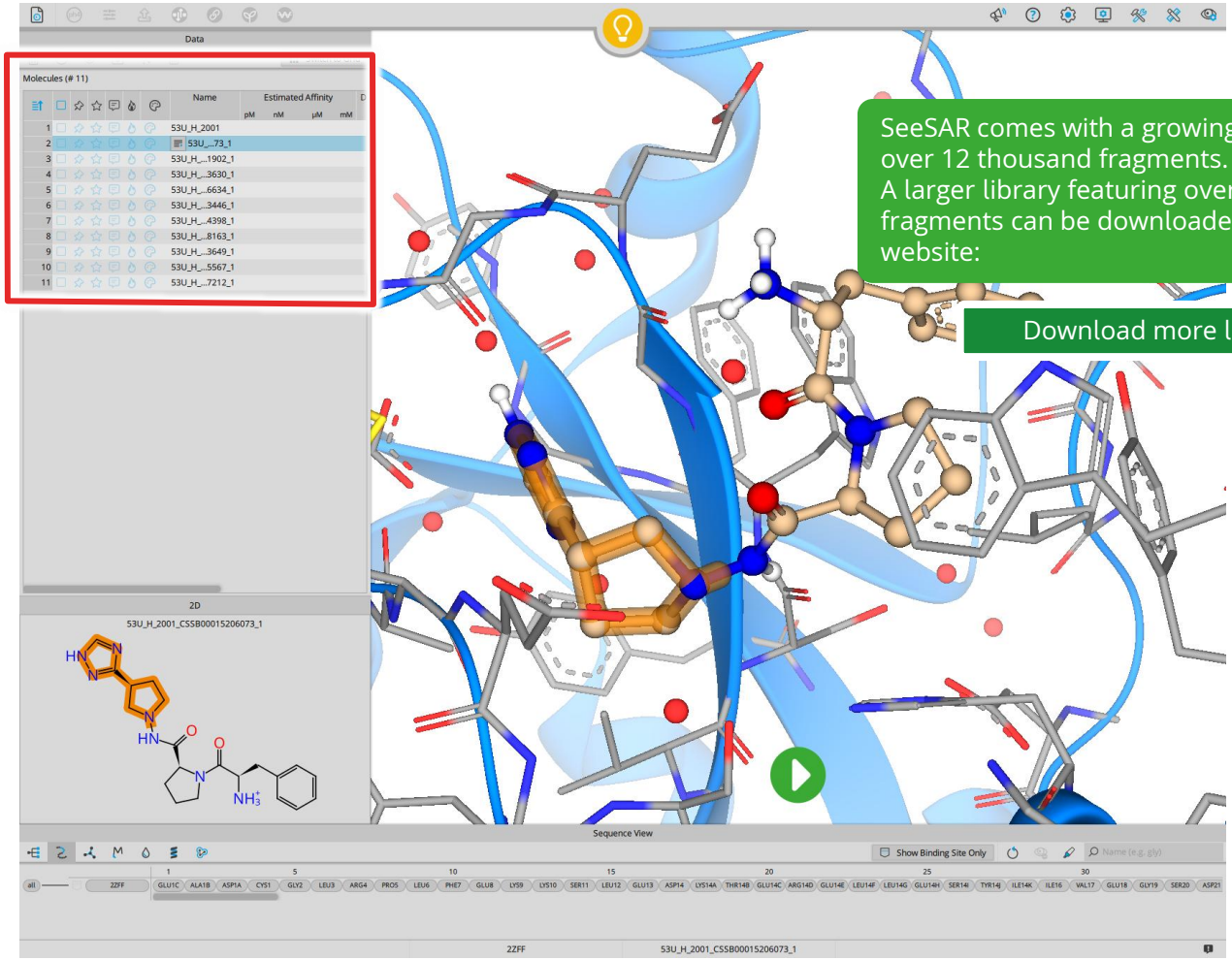
FastGrow:
To grow into a binding site, select a bond in 2D or 3D to select which part of the molecule should be kept. Only one selection is required to perform growing.

Once you made a selection, the “Growing” button will become active. Push it to generate results.



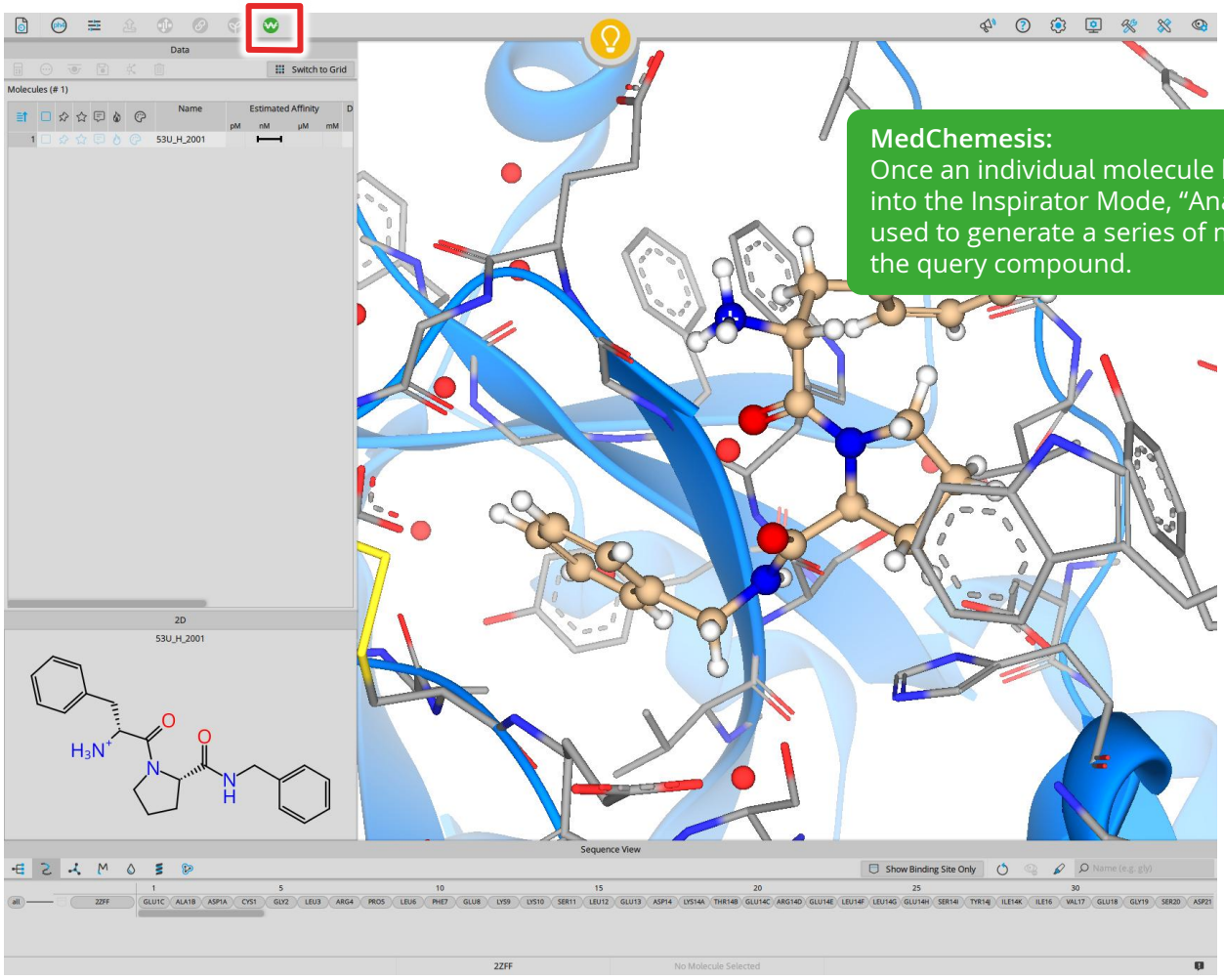
Results will be added to the molecule table. The grown part is highlighted, and the respective name of the used fragment is added to the molecule name.

Note:
It is also possible to grow from a hydrogen in 3D.

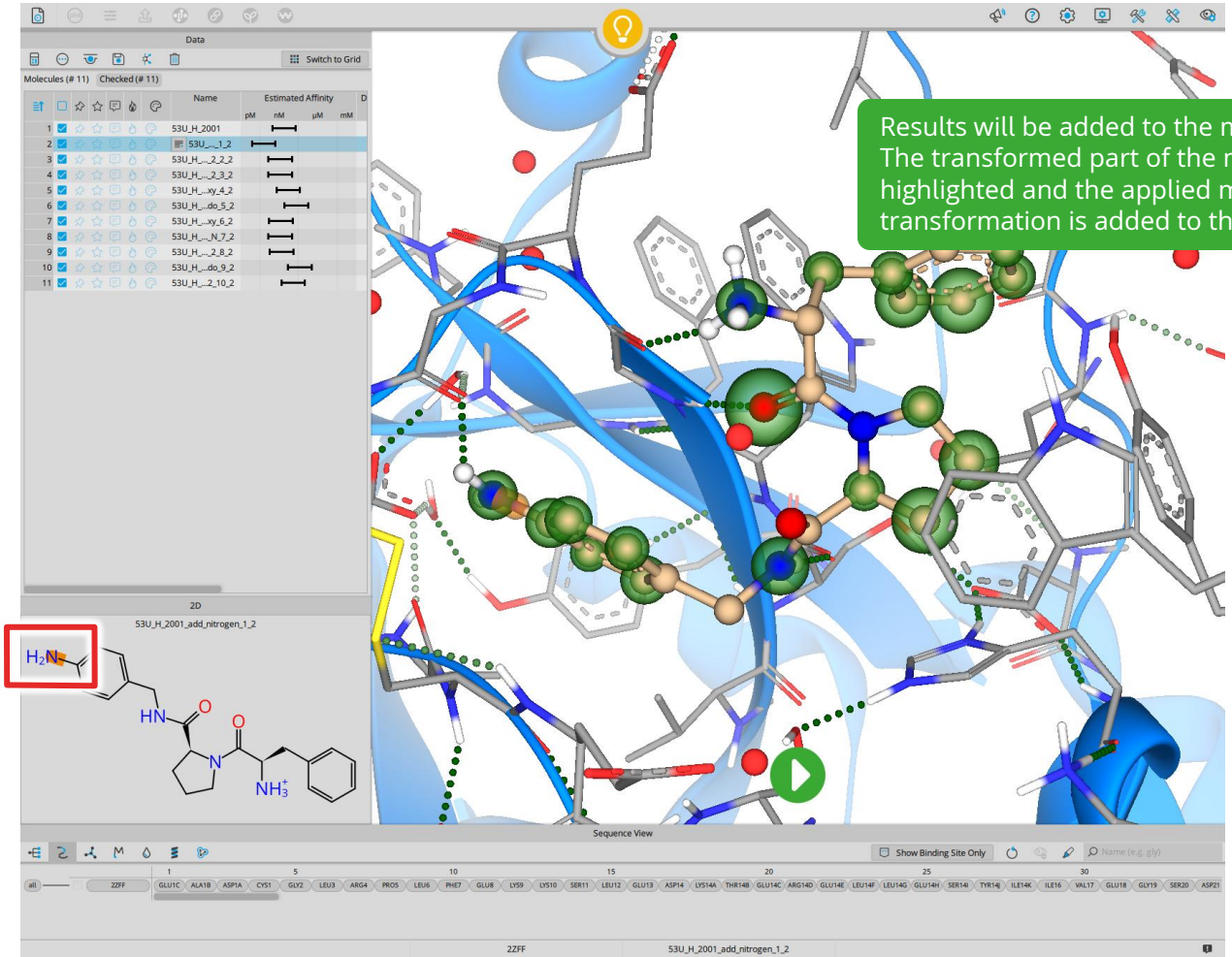


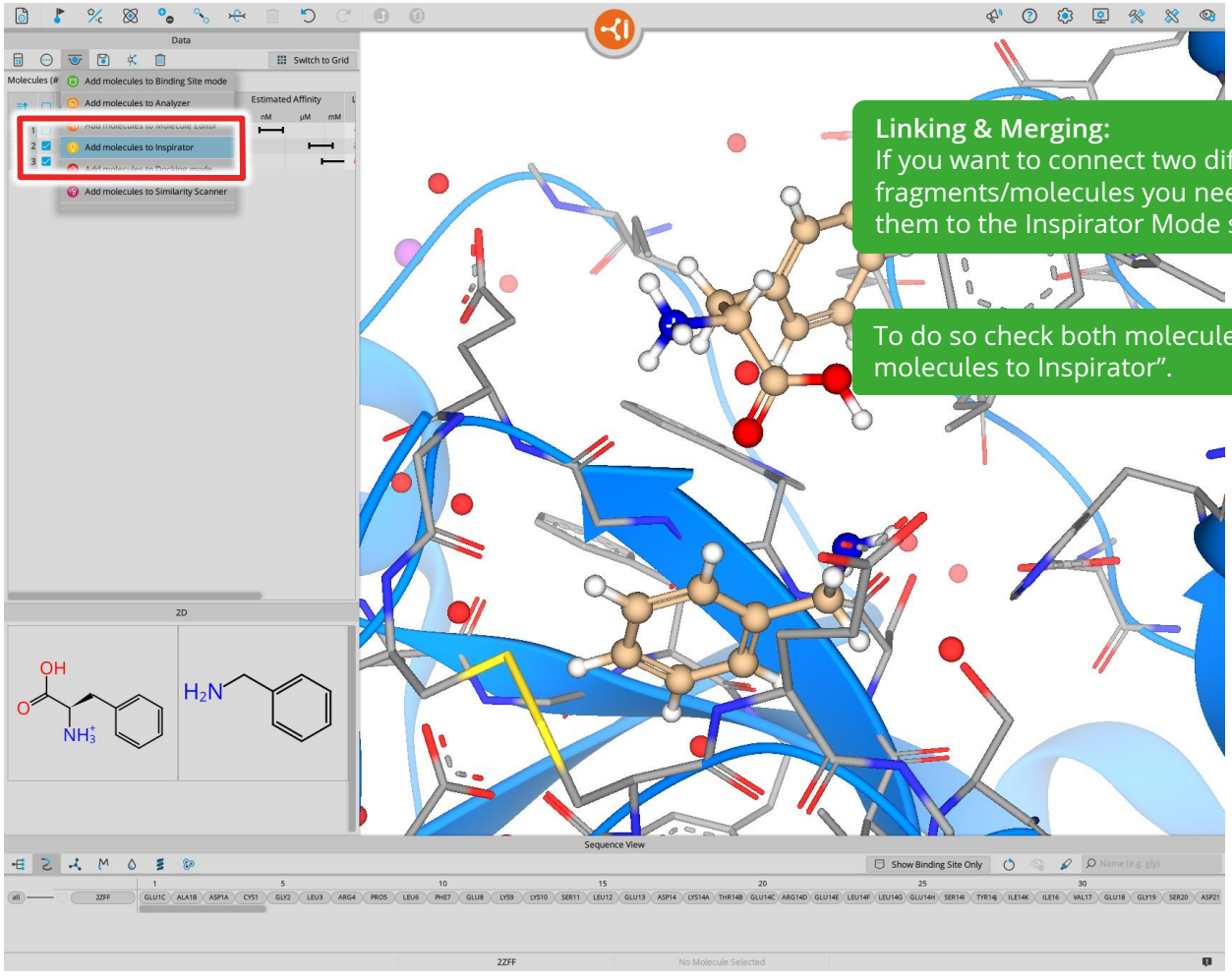
SeeSAR comes with a growing library featuring over 12 thousand fragments.
A larger library featuring over 120 thousand fragments can be downloaded for free from our website:

Download more libraries



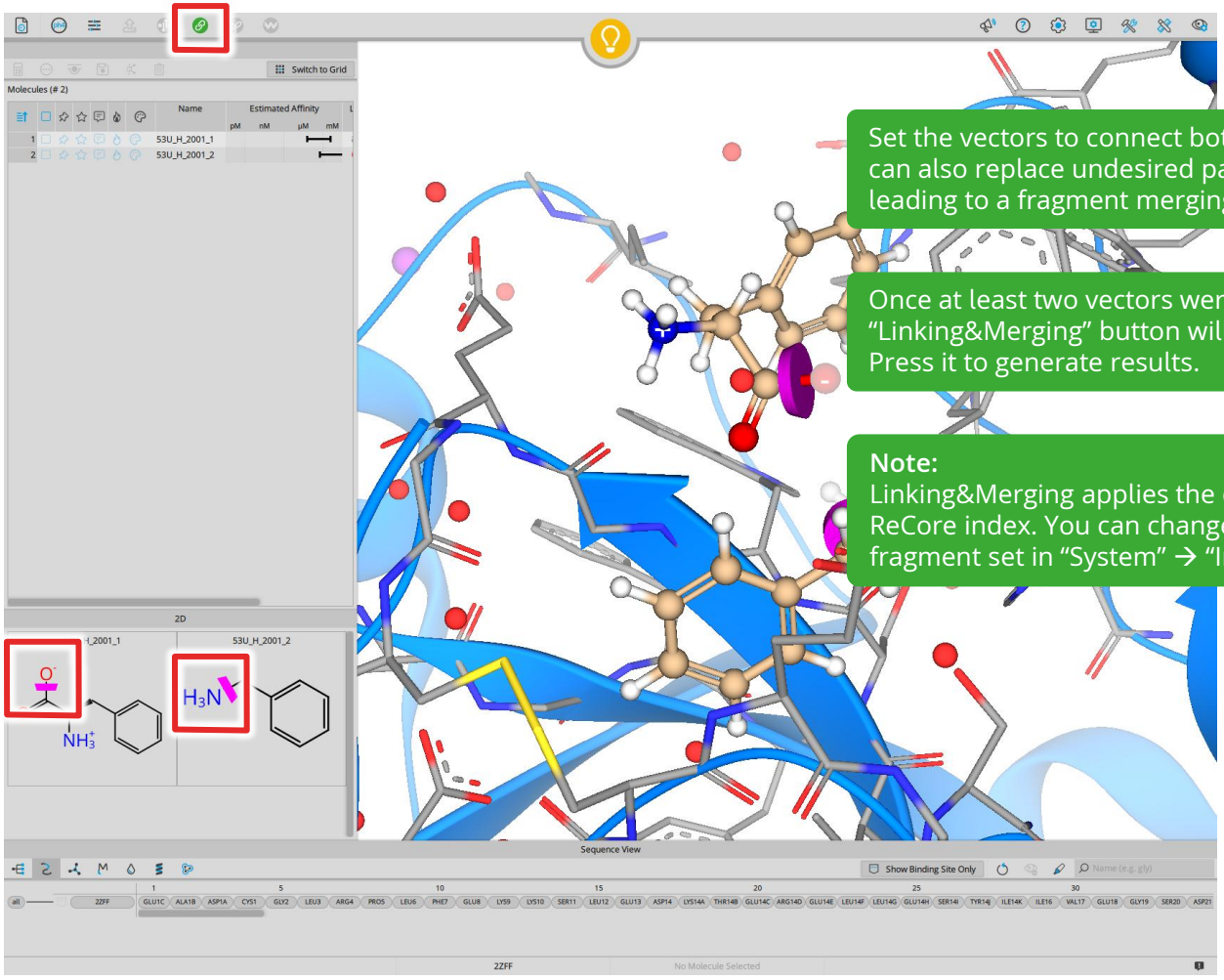
MedChemesis:
Once an individual molecule has been loaded into the Inspirator Mode, “Analoging” can be used to generate a series of molecules based on the query compound.


Data
Switch to Grid
Molecules (# 11)
Checked (# 11)
Name
Estimated Affinity
pM nM µM mM
1 53U_H_2001
2 53U_..._1_2
3 53U_H_..._2_2_2
4 53U_H_..._2_3_2
5 53U_H_..xy_4_2
6 53U_H_..do_5_2
7 53U_H_..xy_6_2
8 53U_H_..._N_7_2
9 53U_H_..._2_8_2
10 53U_H_..do_9_2
11 53U_H_..._2_10_2
2D
53U_H_2001_add_nitrogen_1_2
Results will be added to the molecule table.
The transformed part of the molecule will be highlighted and the applied medicinal chemistry transformation is added to the molecule name.
Sequence View
Show Binding Site Only
2ZFF
53U_H_2001_add_nitrogen_1_2



Linking & Merging:
If you want to connect two different fragments/molecules you need to load both of them to the Inspirator Mode simultaneously.

To do so check both molecules and select “Add molecules to Inspirator”.

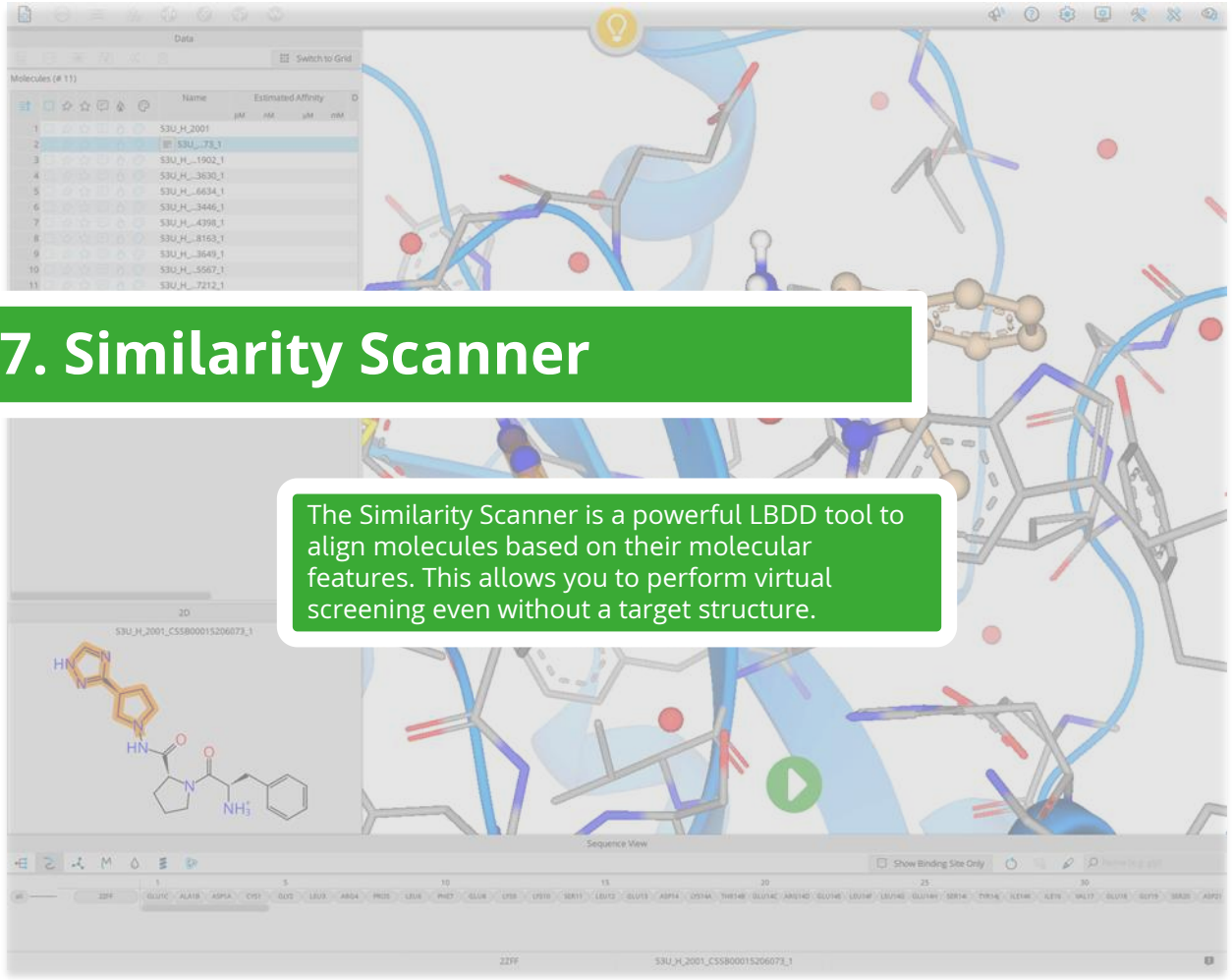


Set the vectors to connect both molecules. You can also replace undesired parts in the process leading to a fragment merging.

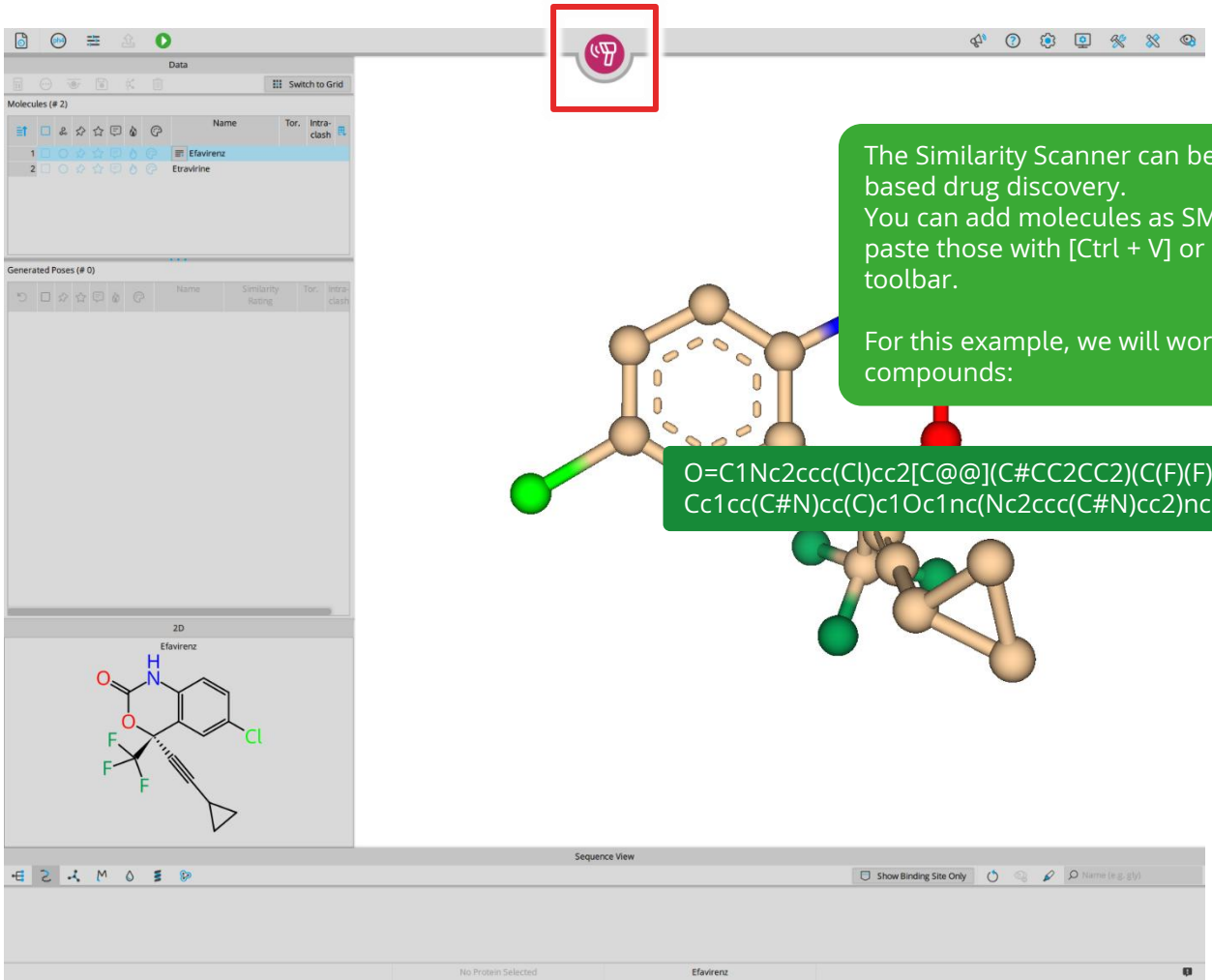
Once at least two vectors were set, the “Linking&Merging” button will become active. Press it to generate results.

Note:
Linking&Merging applies the current active ReCore index. You can change the used fragment set in “System” → “Inspirator”.

7. Similarity Scanner



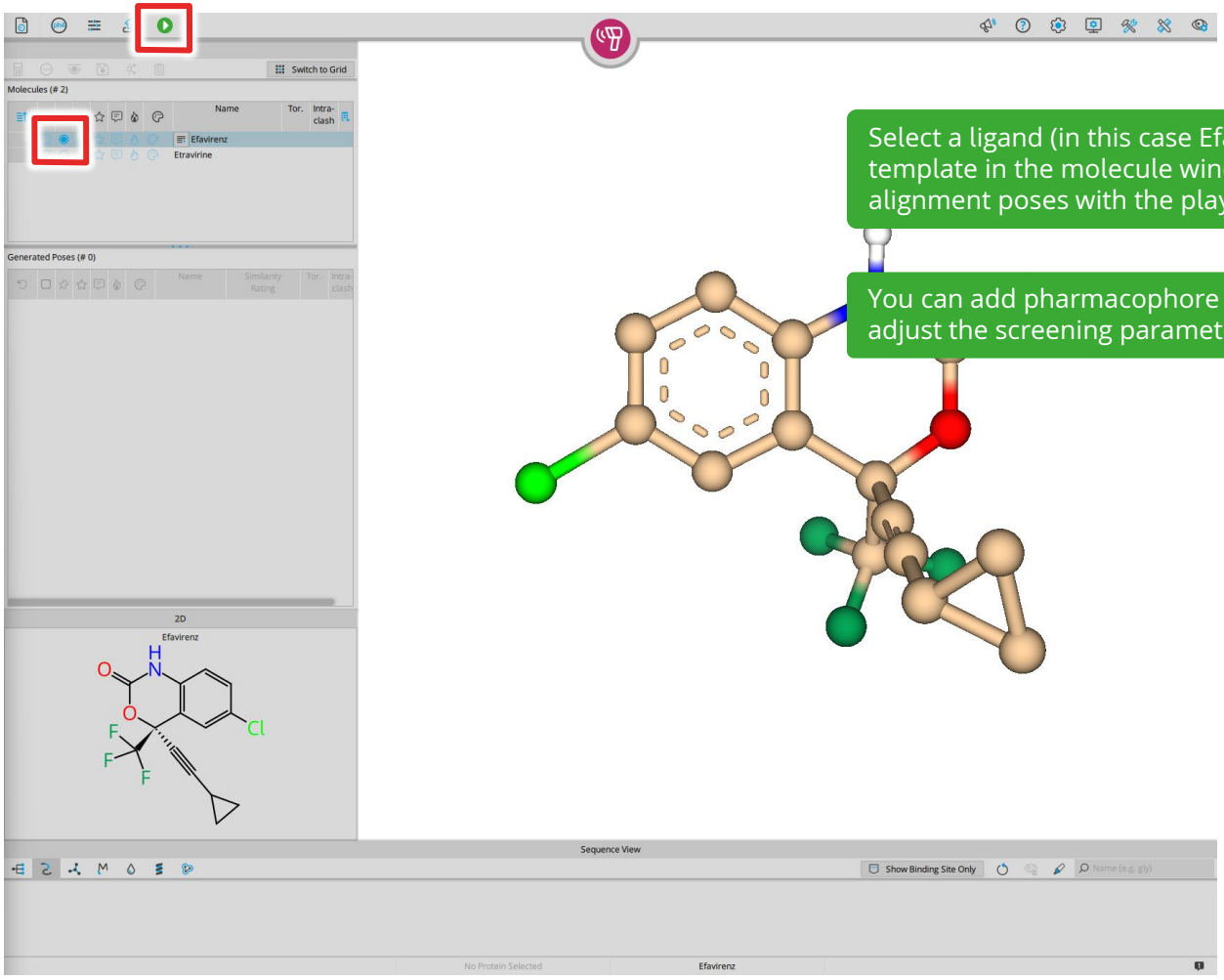
The Similarity Scanner is a powerful LBDD tool to align molecules based on their molecular features. This allows you to perform virtual screening even without a target structure.



The Similarity Scanner can be used for liband-based drug discovery.
You can add molecules as SMILES by copy-and-paste those with [Ctrl + V] or load those via the toolbar.

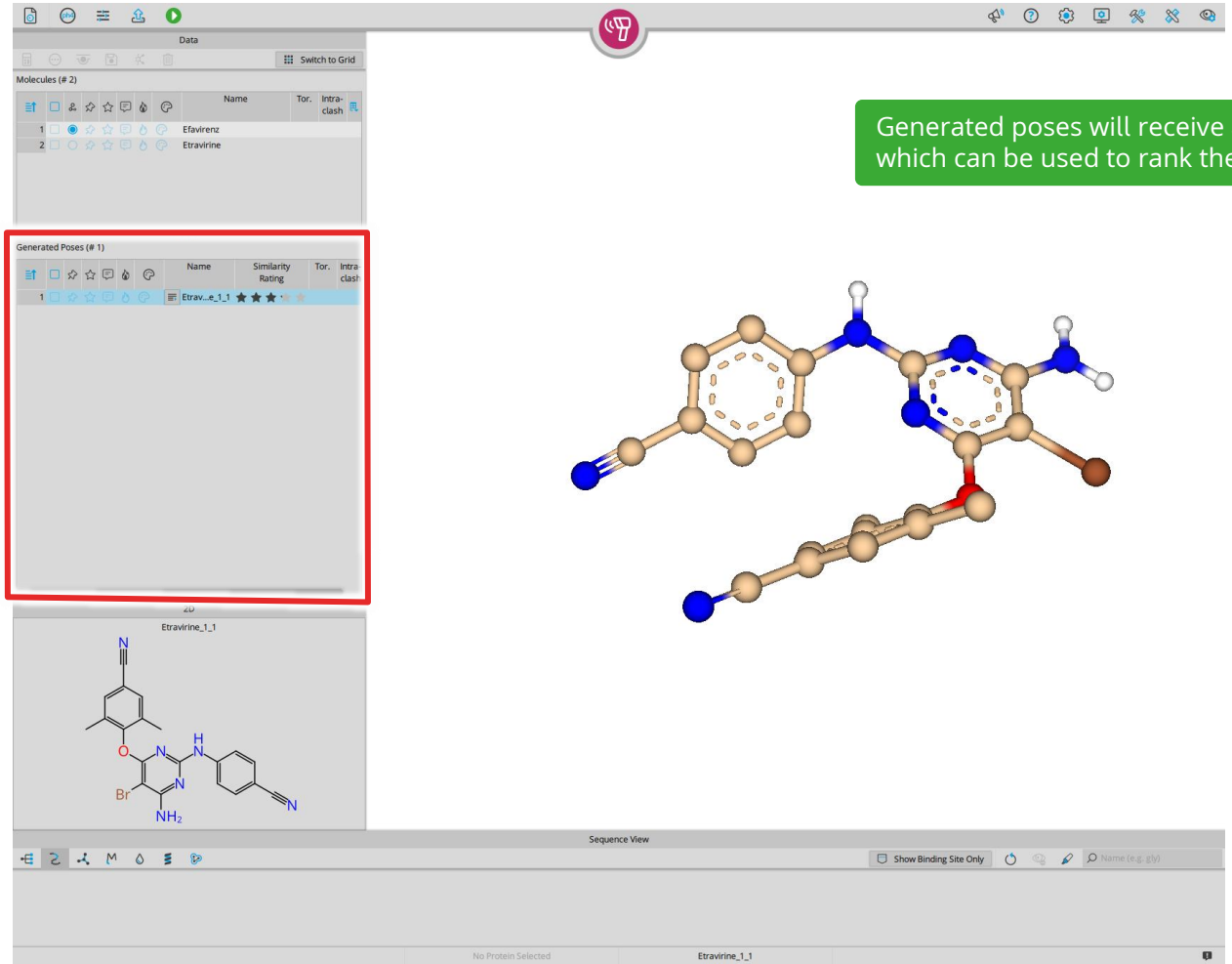
For this example, we will work with two compounds:

O=C1Nc2ccc(Cl)cc2[C@@](C#CC2CC2)(C(F)(F)F)O1 Efavirenz
Cc1cc(C#N)cc(C)c1Oc1nc(Nc2ccc(C#N)cc2)nc(N)c1Br Etravirine



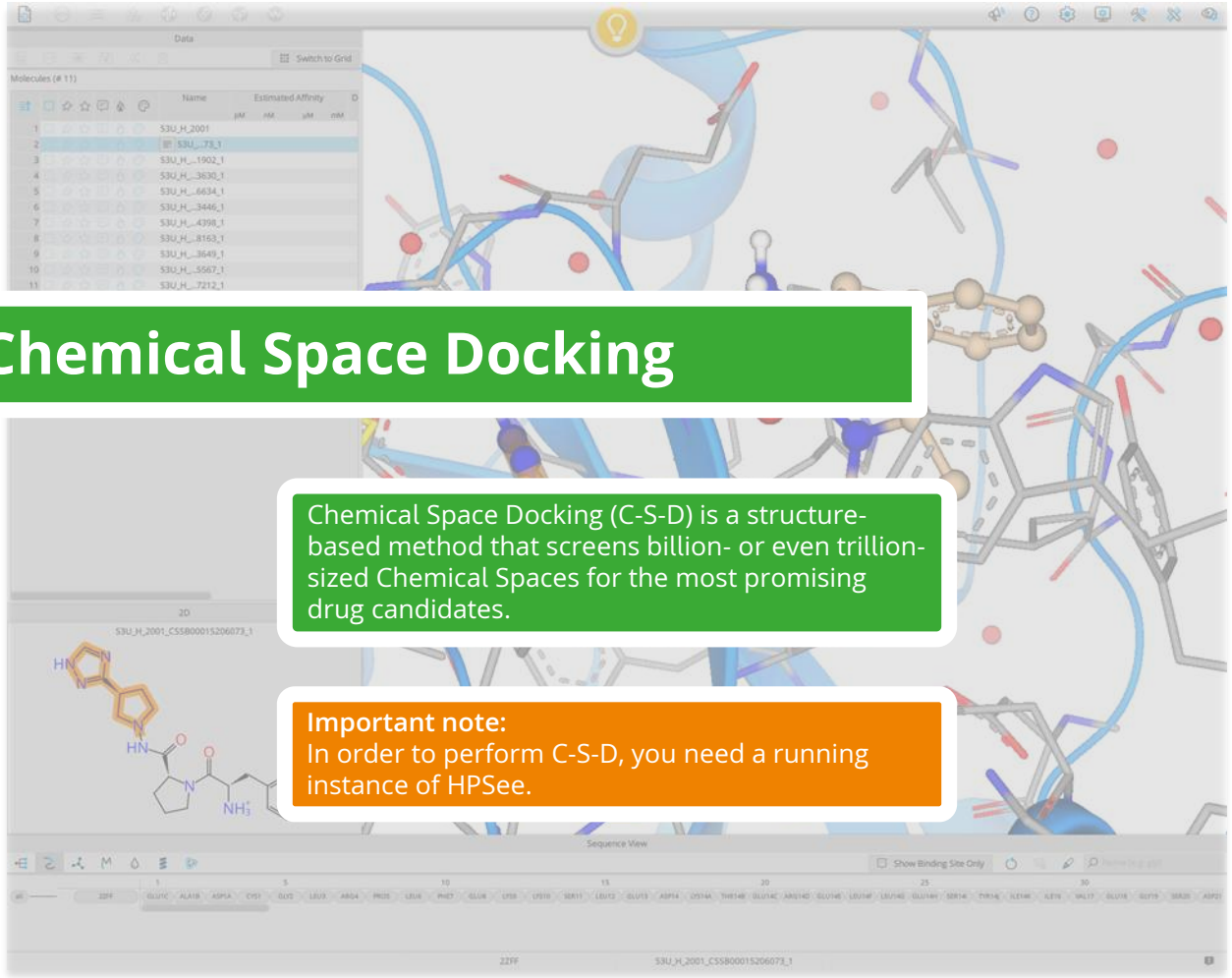
Select a ligand (in this case Efavirenz) as a template in the molecule window. Generate alignment poses with the play button.

You can add pharmacophore constraints and adjust the screening parameters as well.



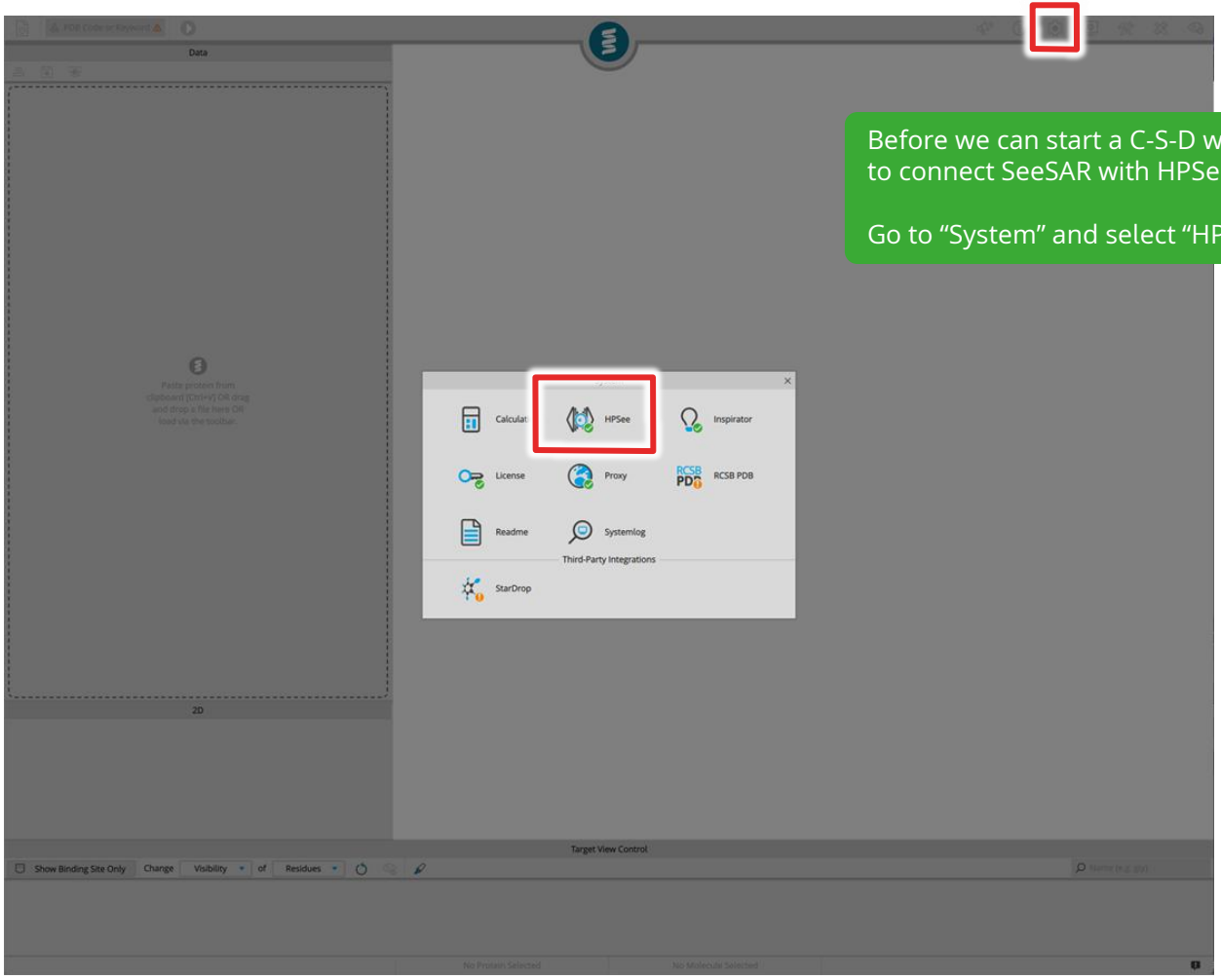
Generated poses will receive an alignment score which can be used to rank the compounds.

8. Chemical Space Docking



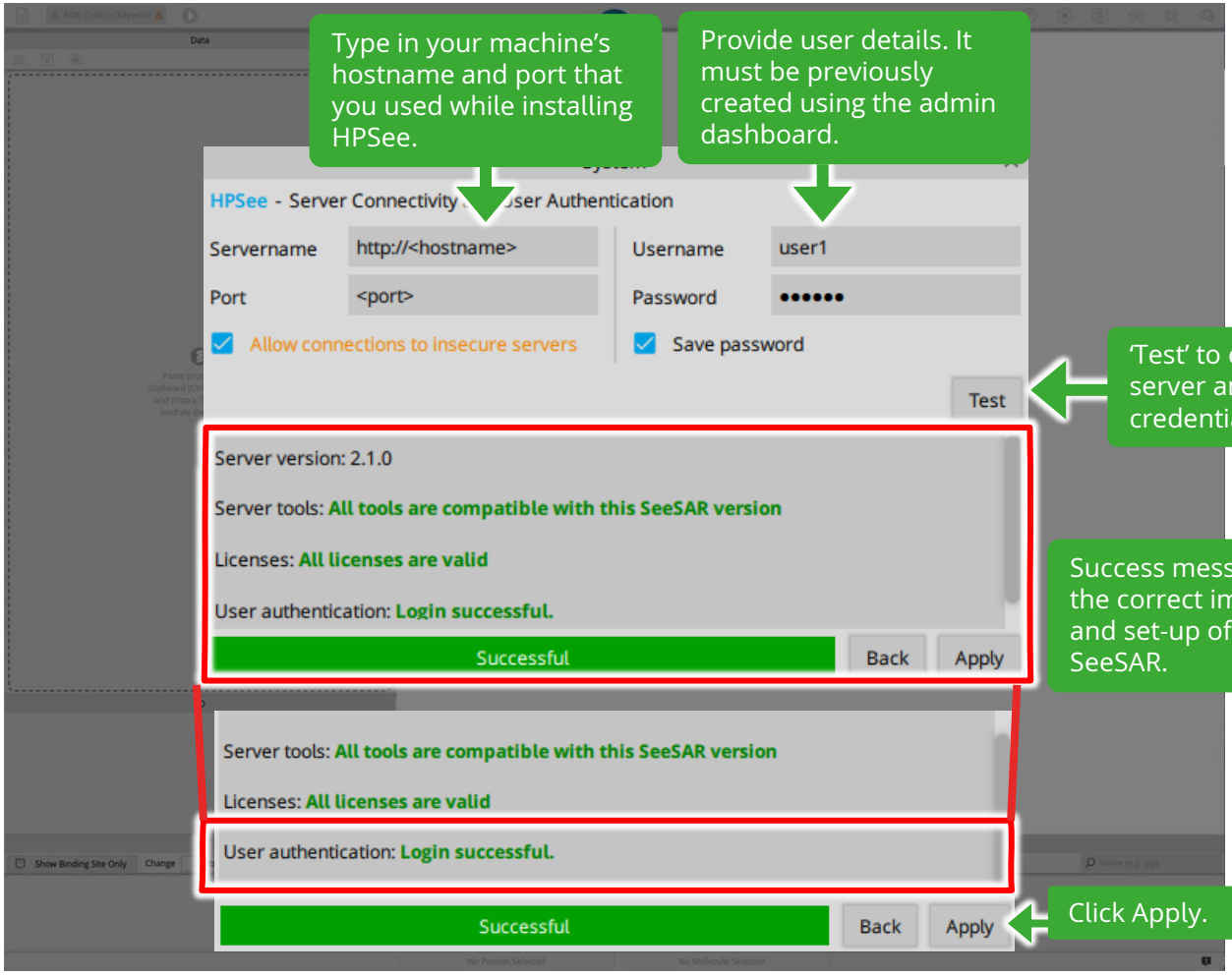
Chemical Space Docking (C-S-D) is a structure-based method that screens billion- or even trillion-sized Chemical Spaces for the most promising drug candidates.

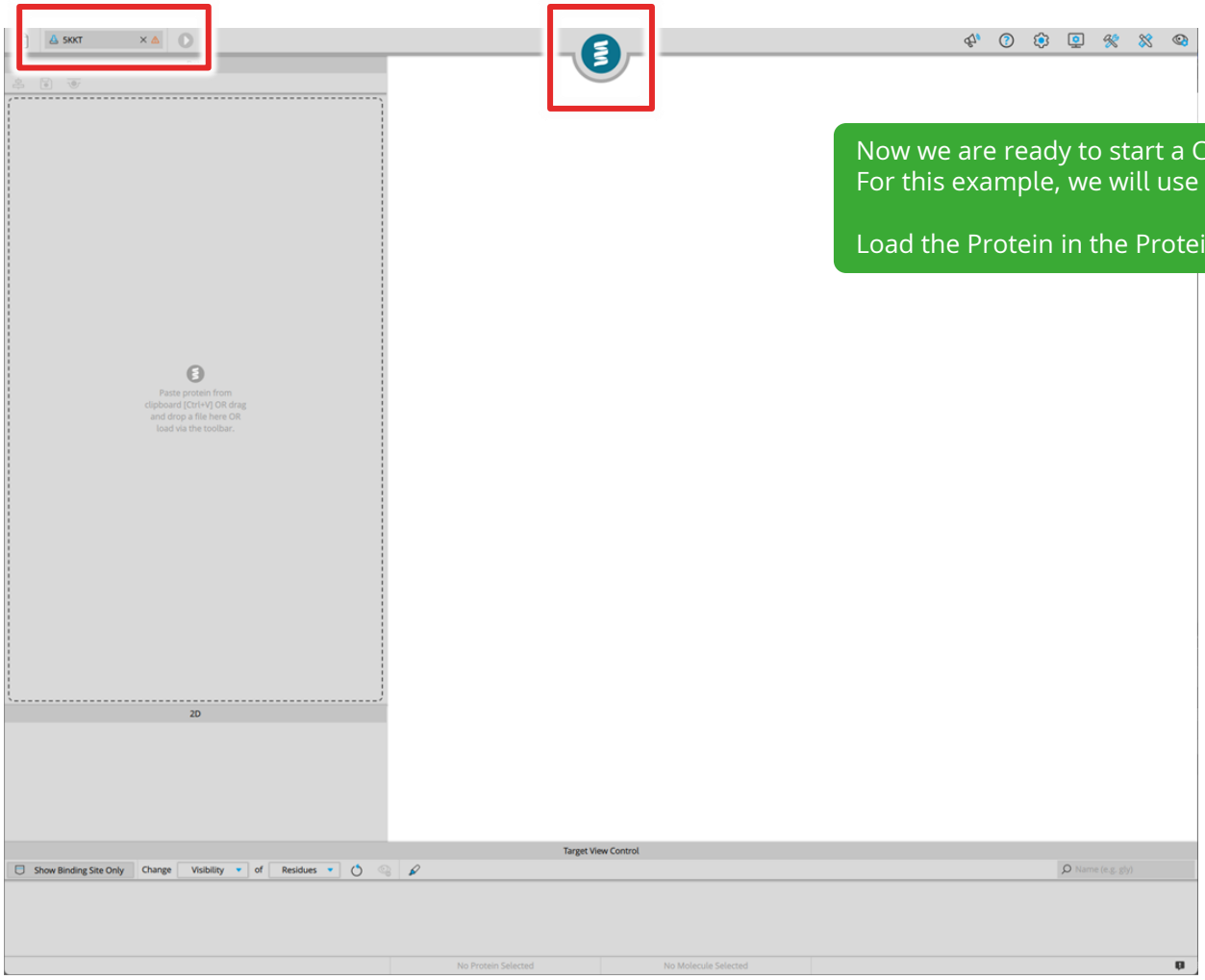
Important note:
In order to perform C-S-D, you need a running instance of HPSee.



Before we can start a C-S-D workflow, we need to connect SeeSAR with HPSee.

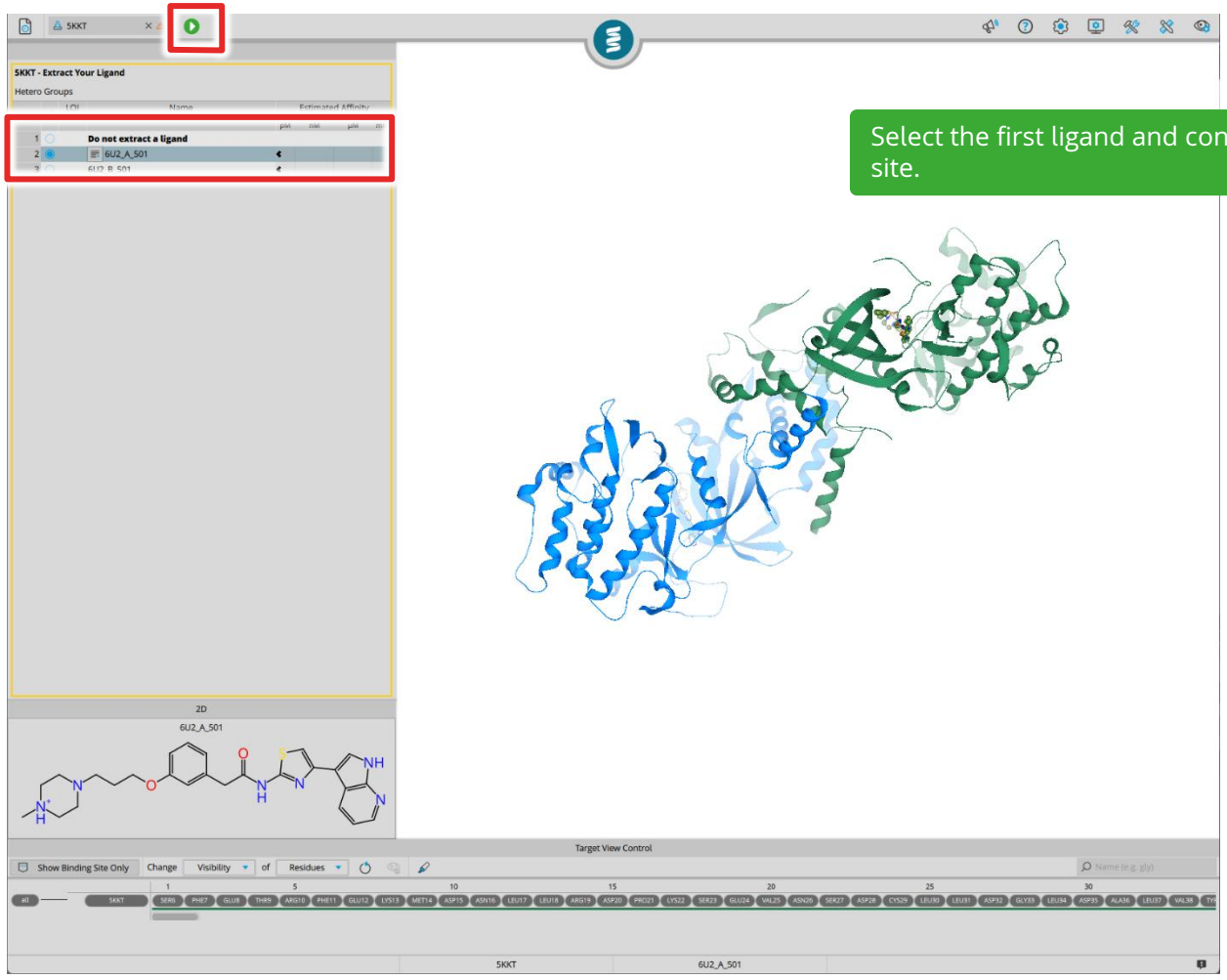
Go to “System” and select “HPSee”.


Type in your machine's hostname and port that you used while installing HPSee.
Provide user details. It must be previously created using the admin dashboard.
HPSee - Server Connectivity
User Authentication
Servername
http://<hostname>
Username
user1
Port
<port>
Password
Allow connections to insecure servers
Save password
Test
'Test' to check validity of server and login credentials.
Server version: 2.1.0
Server tools: All tools are compatible with this SeeSAR version
Licenses: All licenses are valid
User authentication: Login successful.
Successful
Back
Apply
Success message indicates the correct implementation and set-up of HPSee and SeeSAR.
Server tools: All tools are compatible with this SeeSAR version
Licenses: All licenses are valid
User authentication: Login successful.
Successful
Back
Apply
Click Apply.

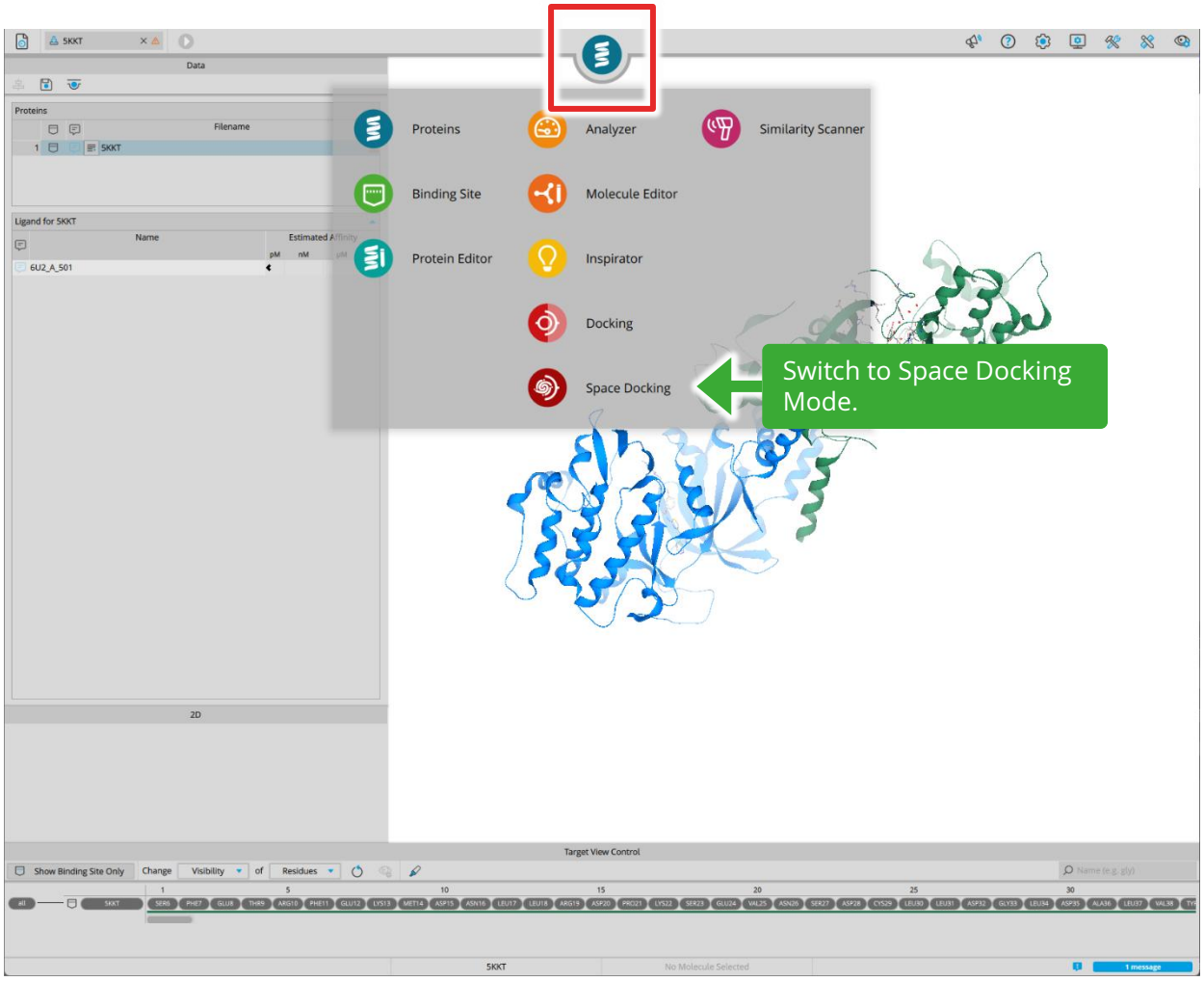


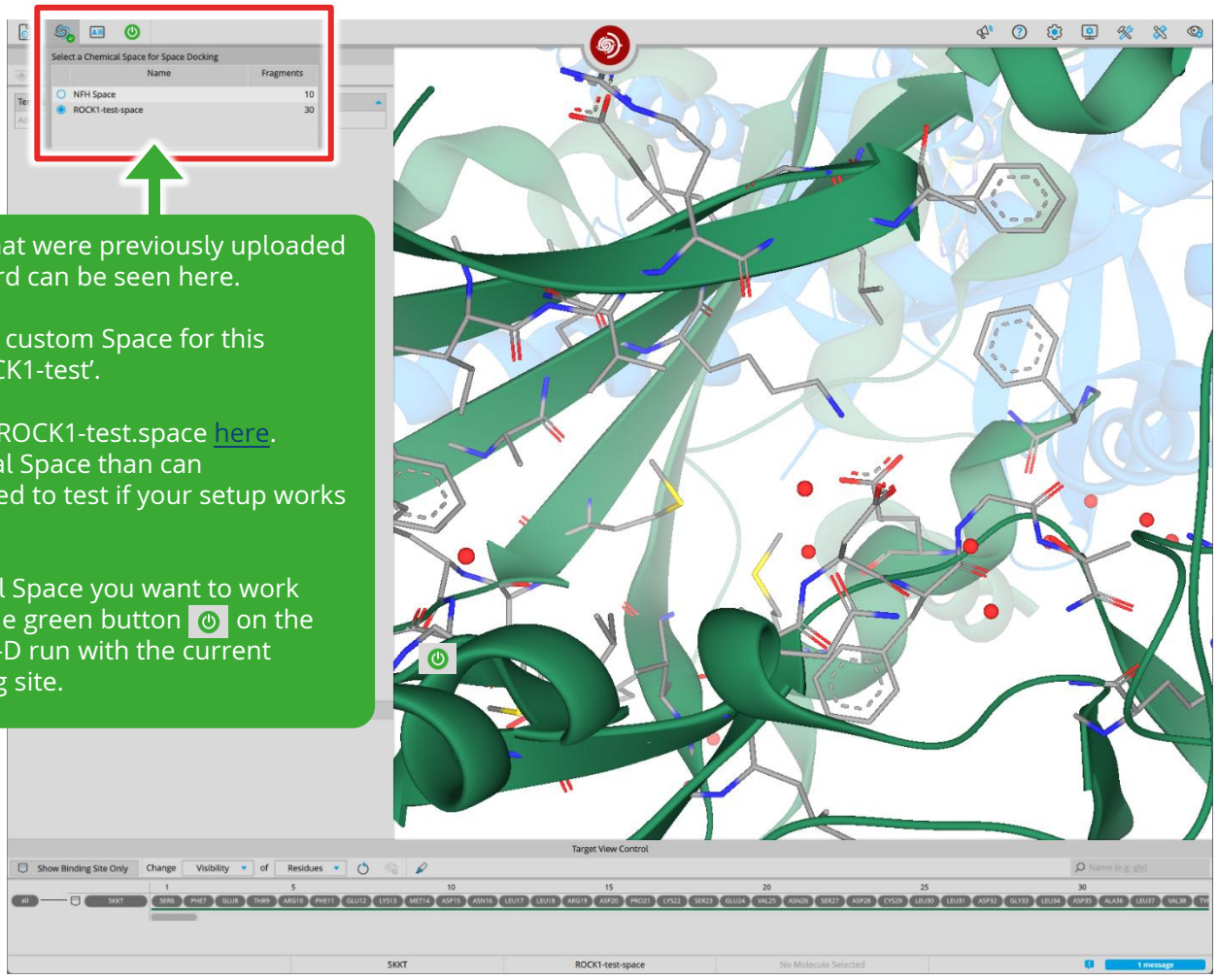
Now we are ready to start a C-S-D run.
For this example, we will use 5KKT as PDB.

Load the Protein in the Protein Mode.



Select the first ligand and confirm your binding site.


Proteins
Analyzer
Similarity Scanner
Binding Site
Molecule Editor
Protein Editor
Inspirator
Docking
Space Docking
Switch to Space Docking Mode.

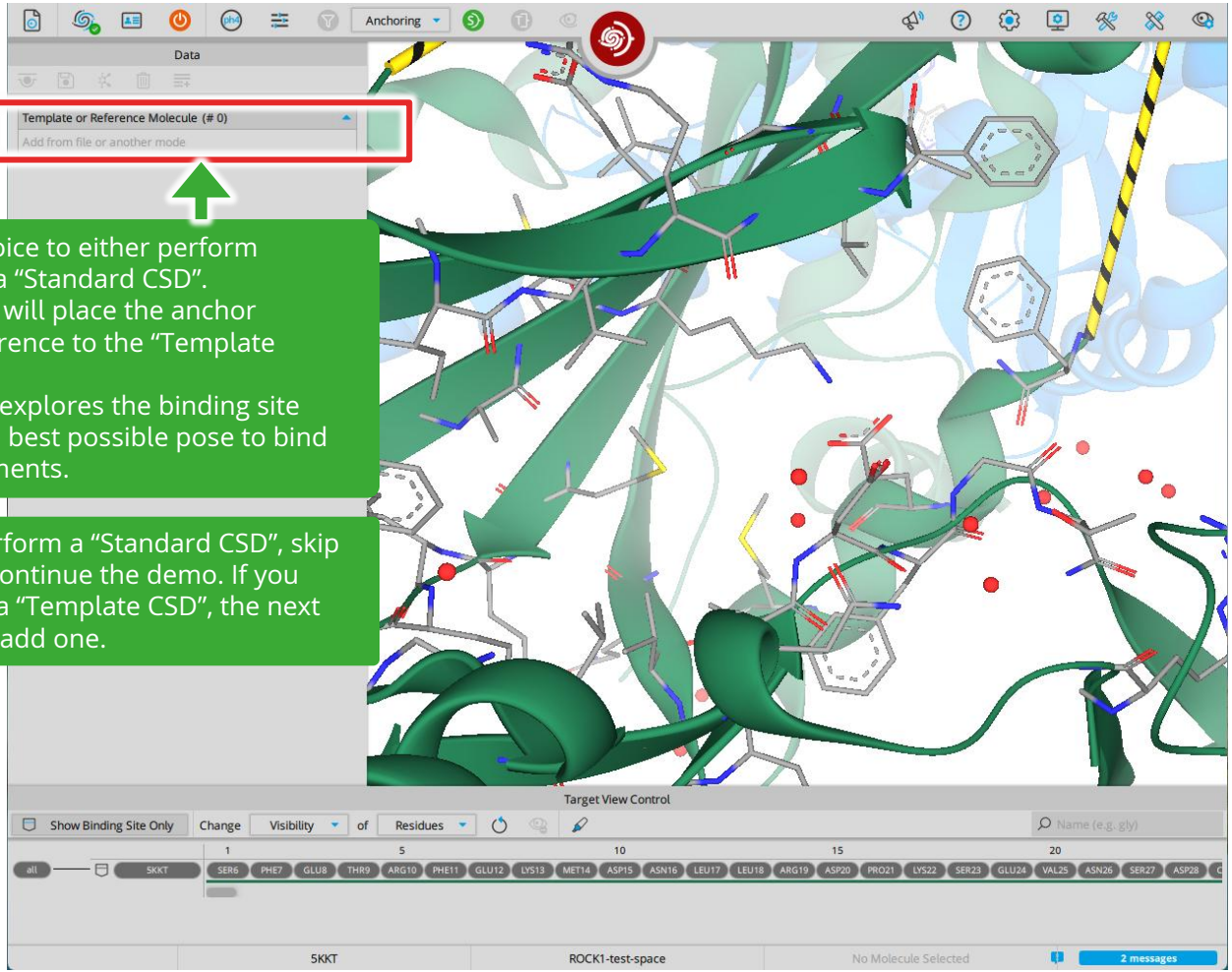


Chemical Spaces that were previously uploaded using the Dashboard can be seen here.

We will use a small custom Space for this tutorial, called 'ROCK1-test'.

You download the ROCK1-test.space here.
It's a small Chemical Space than can conveniently be used to test if your setup works as intended.

Select the Chemical Space you want to work with and click on the green button on the top to start the C-S-D run with the current protein and binding site.

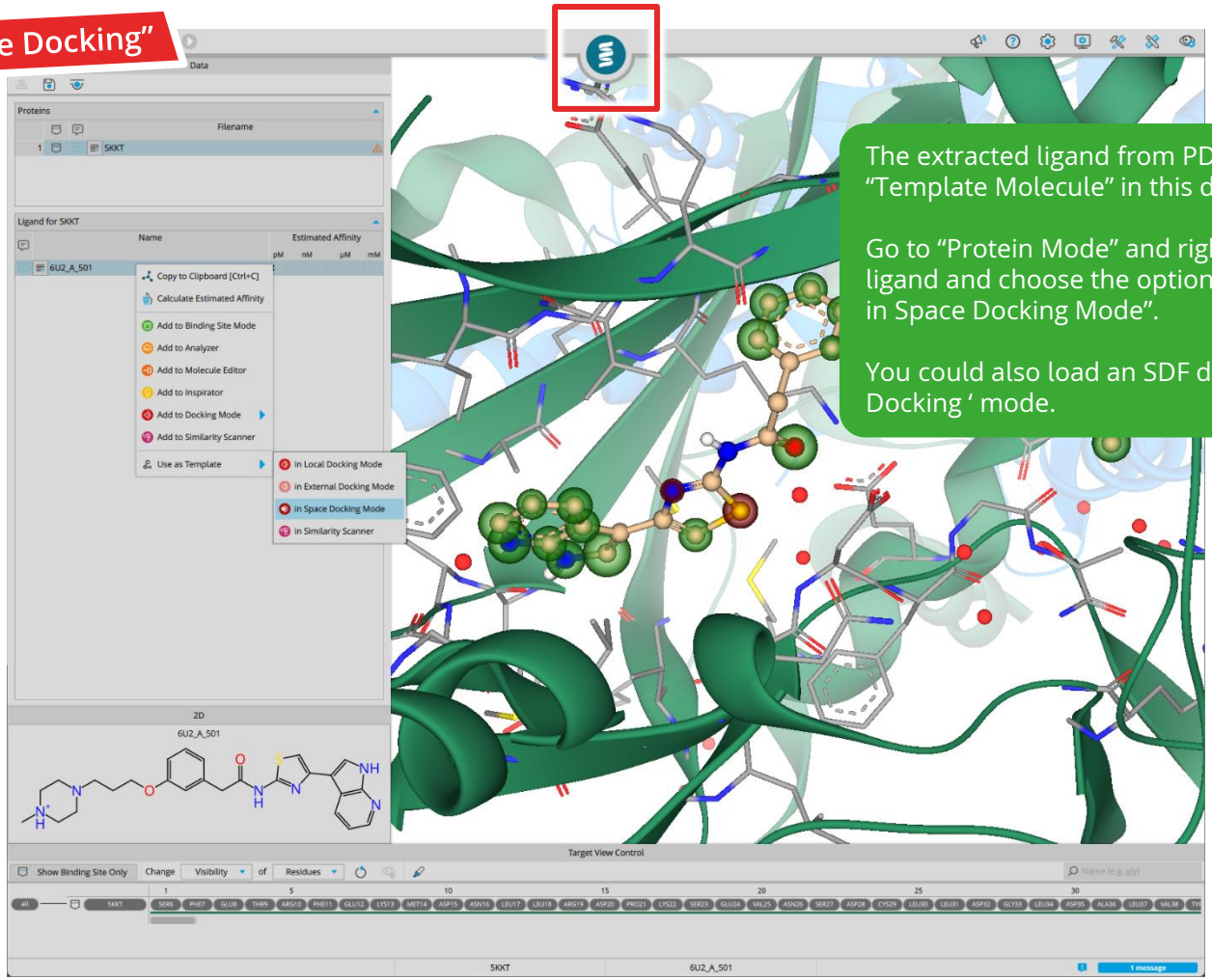


You now have a choice to either perform "Template CSD" or a "Standard CSD".

- **"Template CSD"** will place the anchor fragment in reference to the "Template Molecule".
- **"Standard CSD"** explores the binding site freely to find the best possible pose to bind the anchor fragments.

If you choose to perform a "Standard CSD", skip the next slide and continue the demo. If you choose to perform a "Template CSD", the next slide shows how to add one.

“Template Docking”

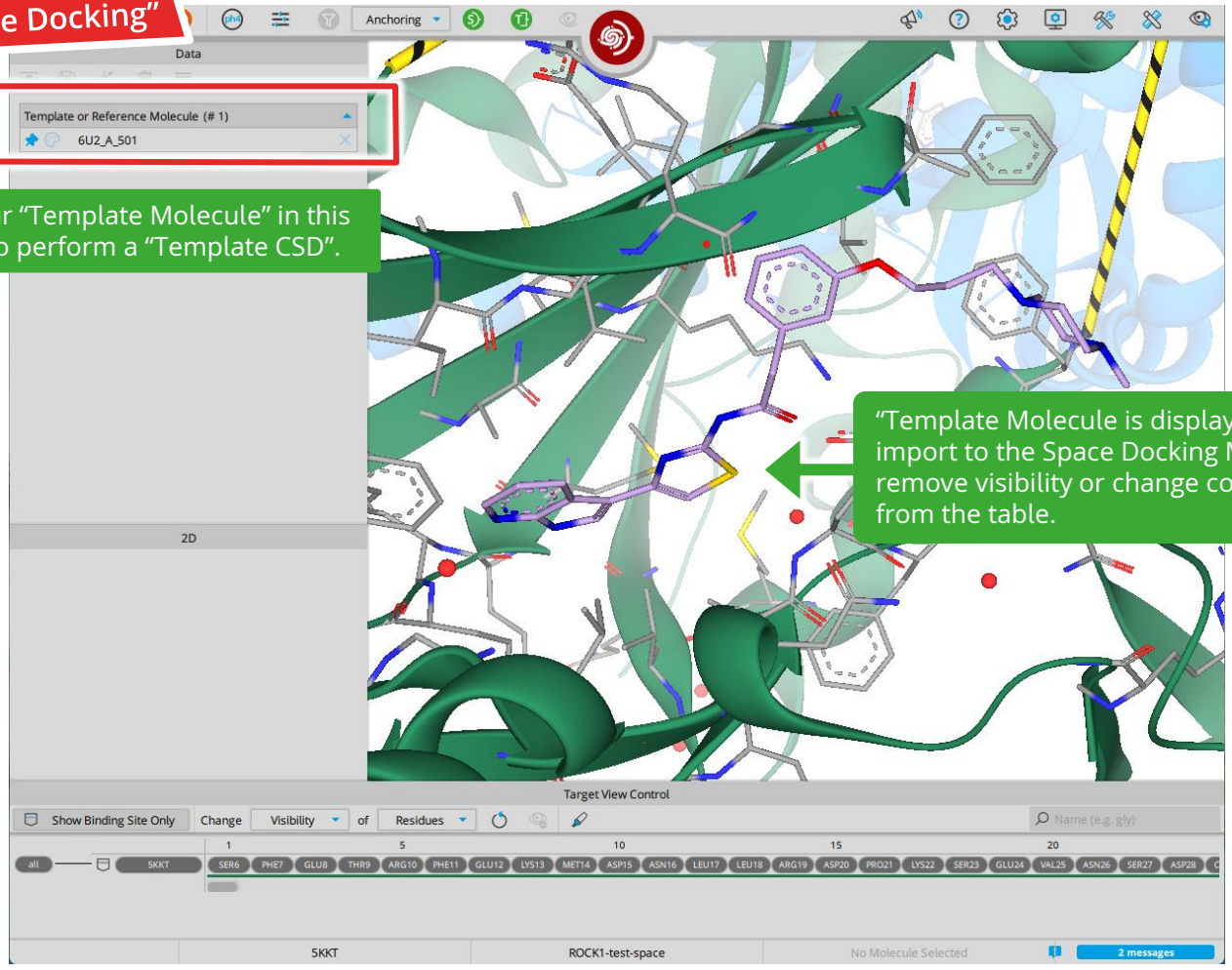


The extracted ligand from PDB can be used as a “Template Molecule” in this demo.

Go to “Protein Mode” and right-click on the ligand and choose the option “Use as Template in Space Docking Mode”.

You could also load an SDF directly in ‘Space Docking ‘ mode.

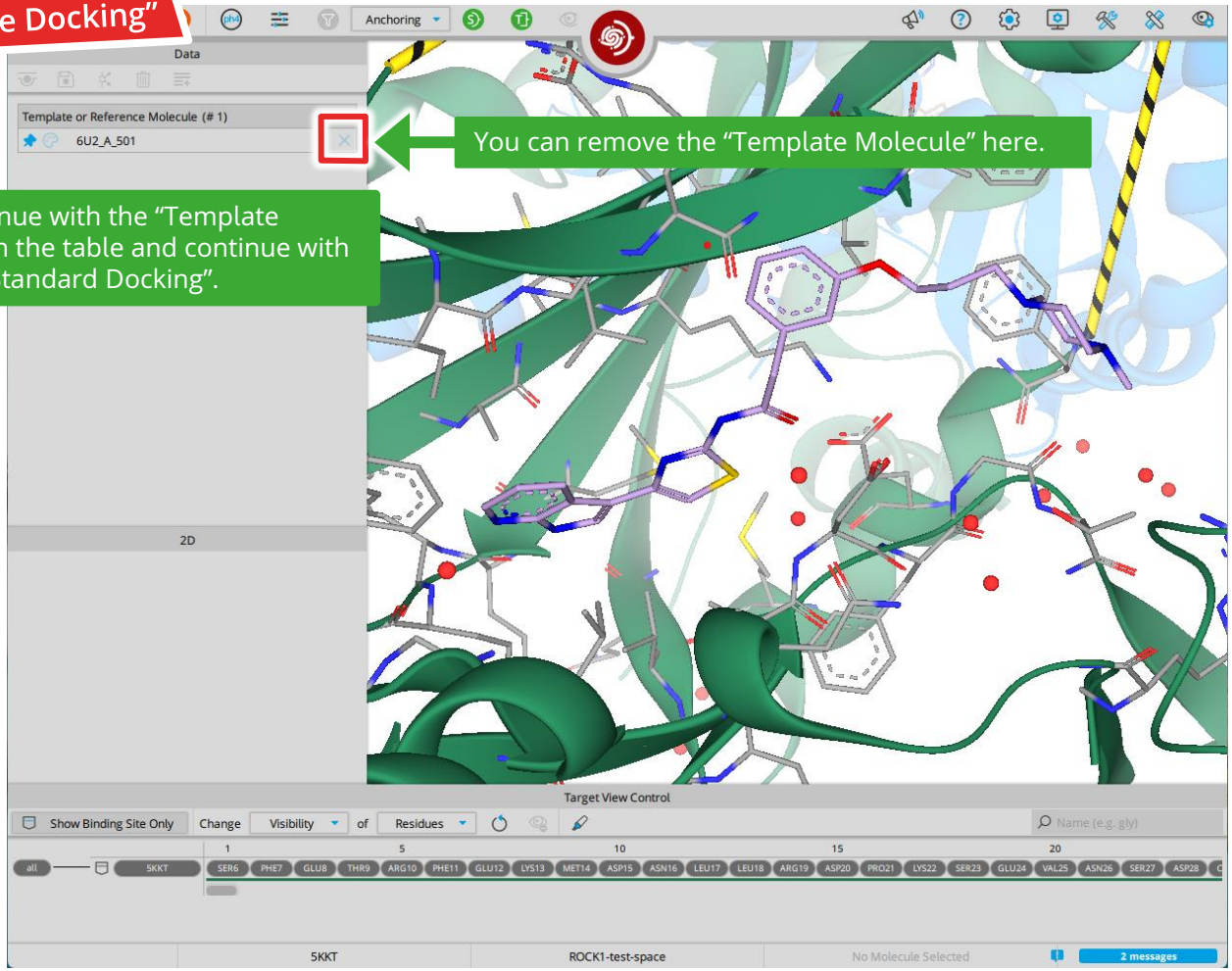
“Template Docking”



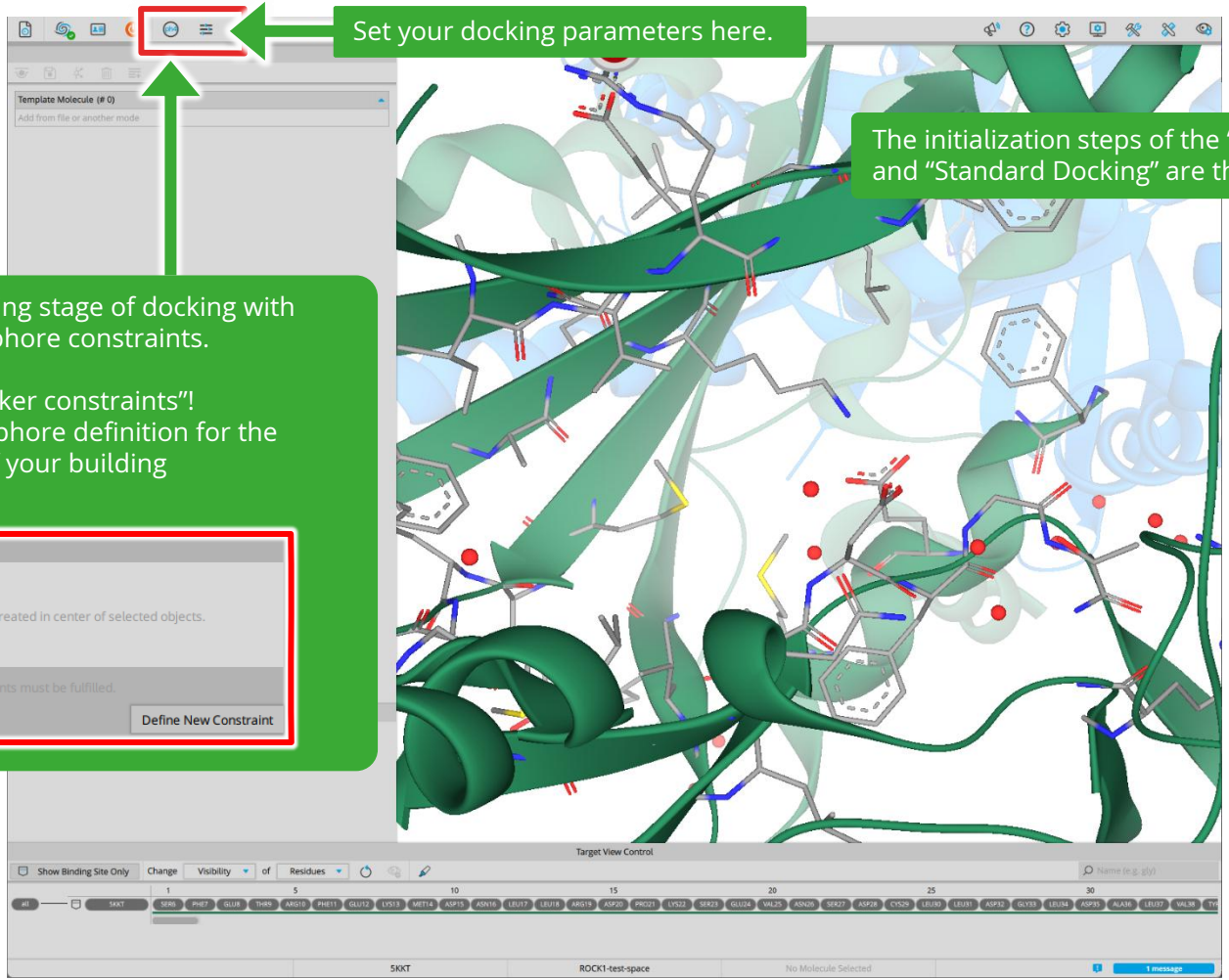
You should see your “Template Molecule” in this box, if you decide to perform a “Template CSD”.

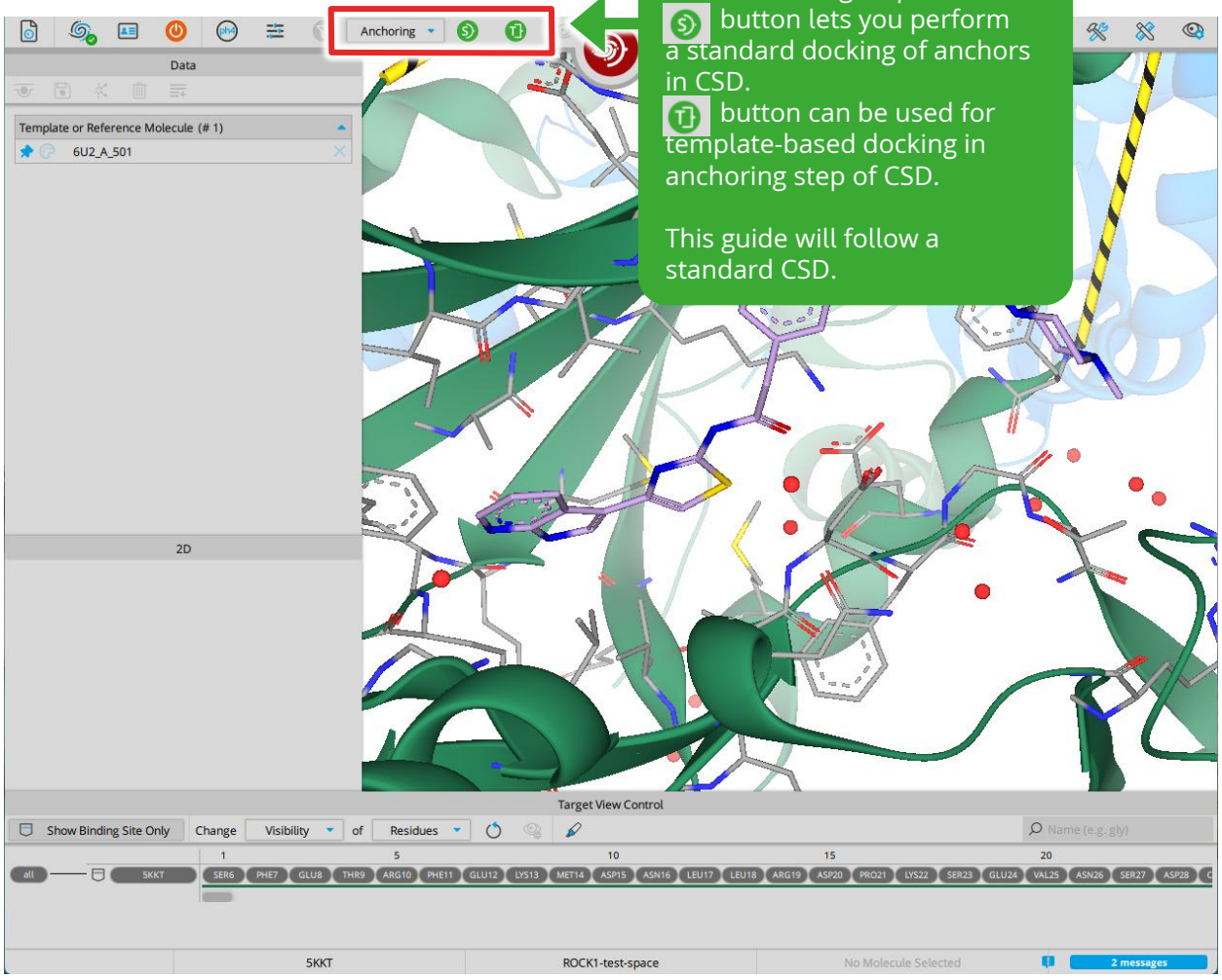
“Template Molecule is displayed in 3D after its import to the Space Docking Mode. You can remove visibility or change color using from the table.

“Template Docking”



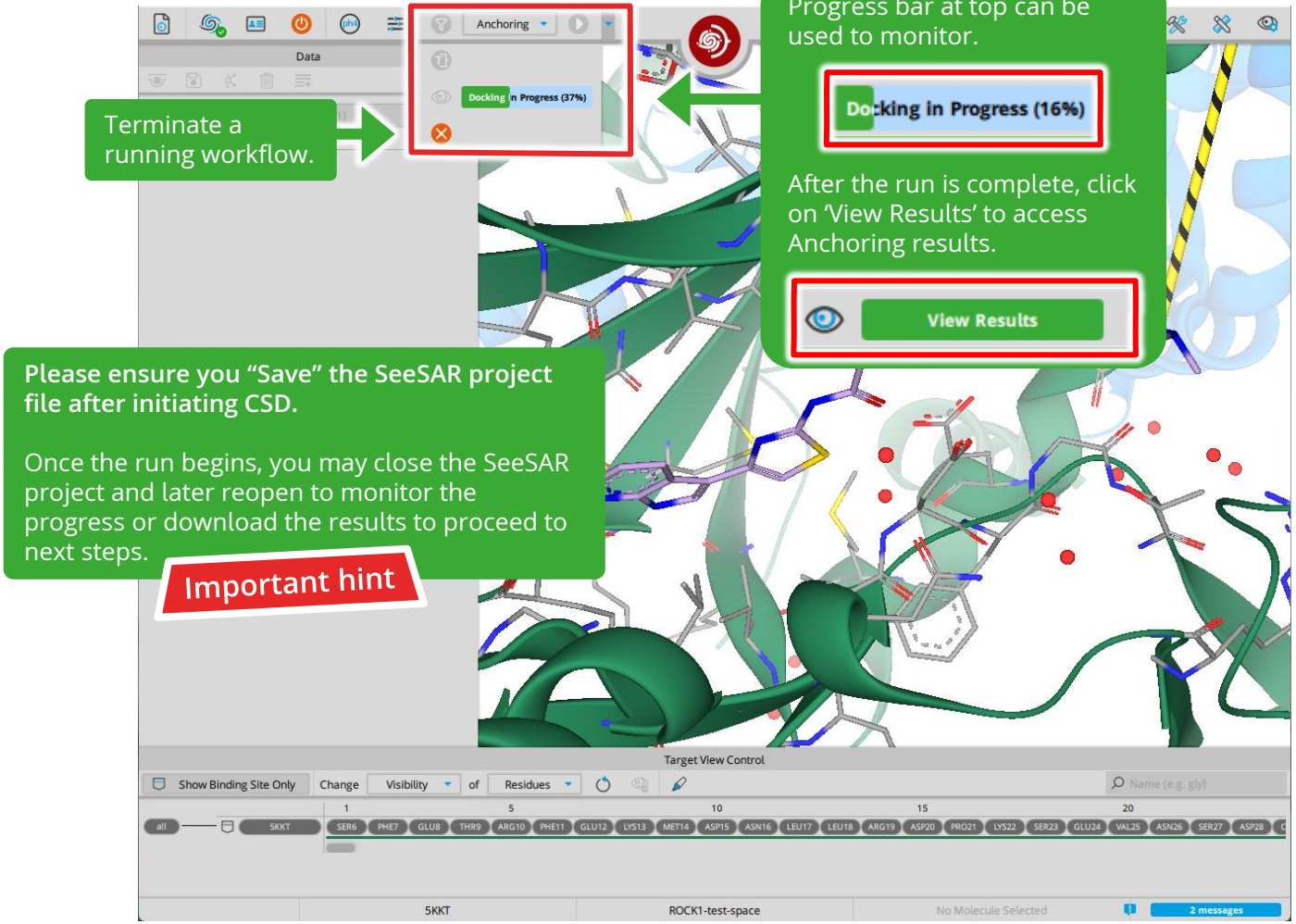
If you want to continue with the “Template Molecule”, keep it in the table and continue with the next slides of “Standard Docking”.

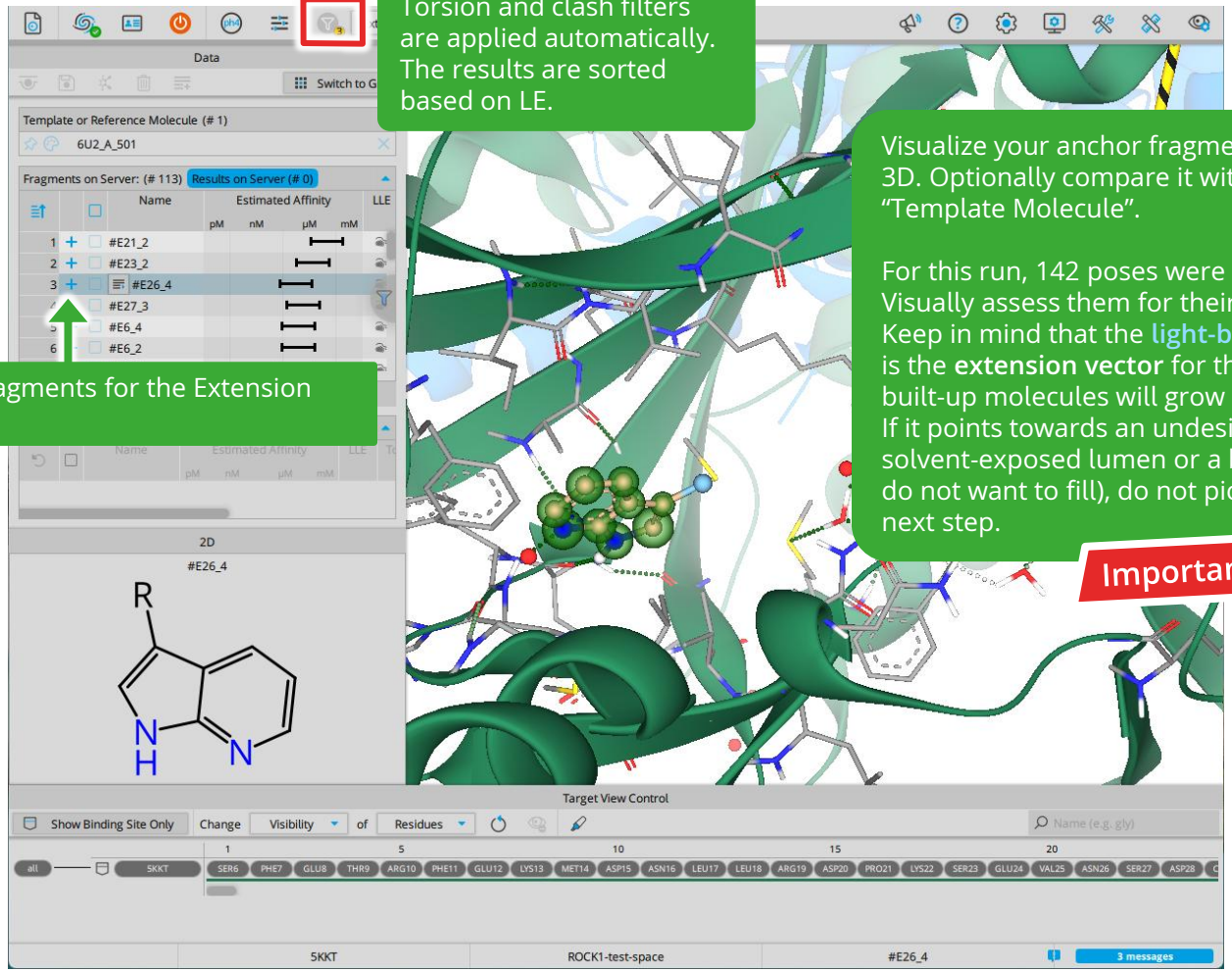

Set your docking parameters here.
The initialization steps of the “Template Docking” and “Standard Docking” are the same.
Guide your Anchoring stage of docking with desired pharmacophore constraints.
Hint: Check out “linker constraints”! This is a pharmacophore definition for the extension vector of your building blocks/synthons.
Define Pharmacophore
New spheres will be created in center of selected objects.
At least 0 optional constraints must be fulfilled.
Define New Constraint
Template Molecule (# 0)
Add from file or another mode
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
5KKT
ROCK1-test-space
No Molecule Selected
1 message

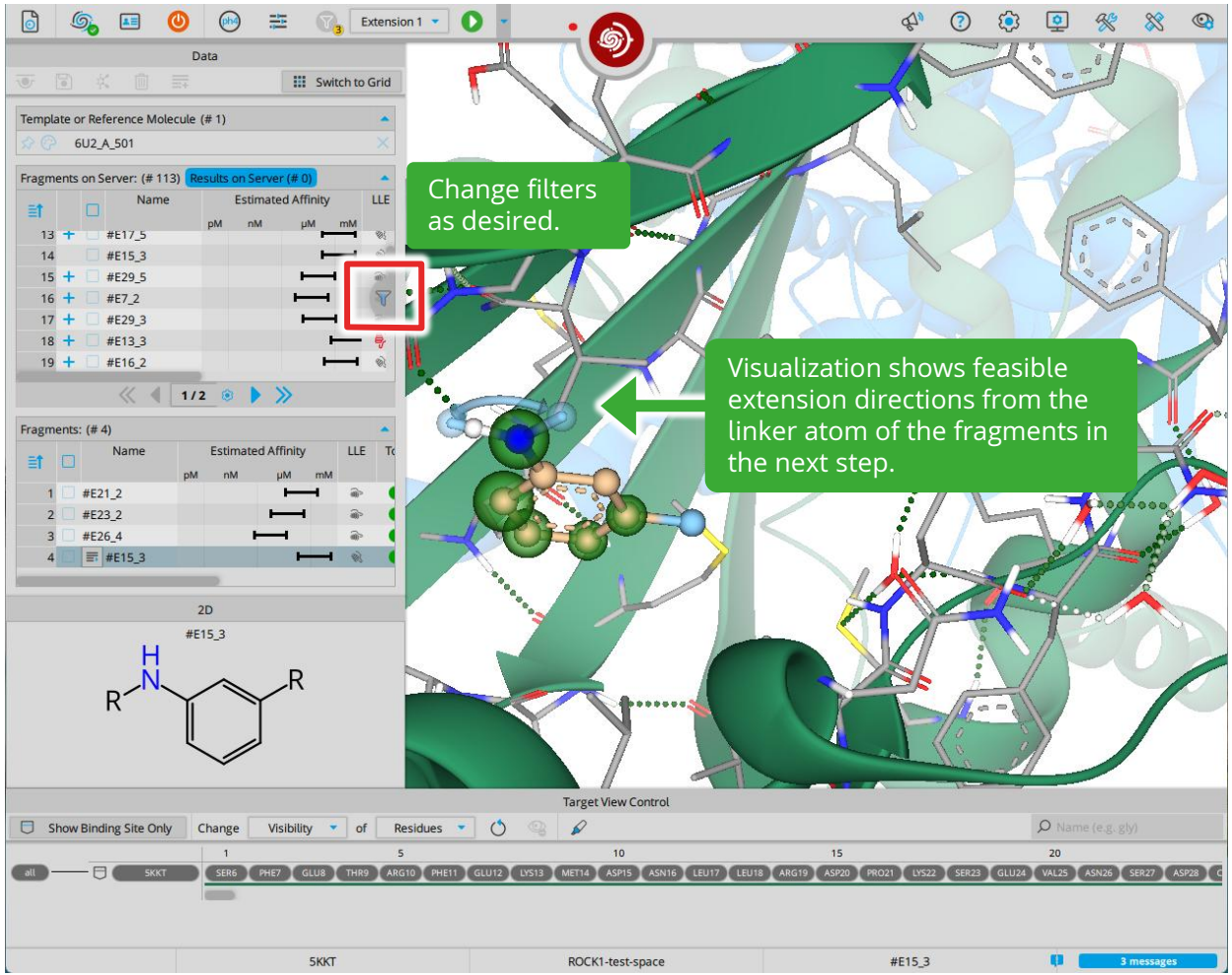


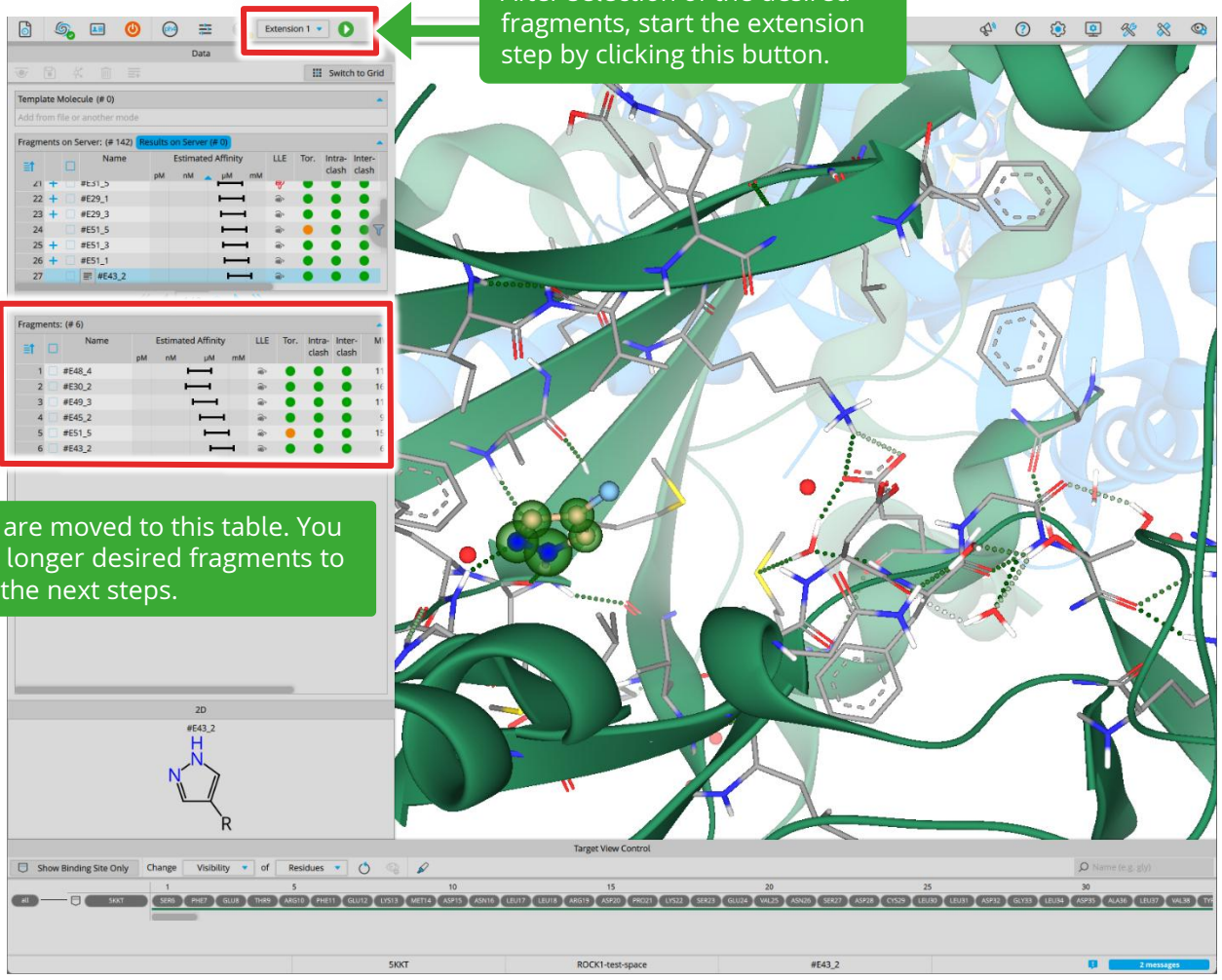
Start Anchoring step of CSD.
button lets you perform a standard docking of anchors in CSD.
button can be used for template-based docking in anchoring step of CSD.

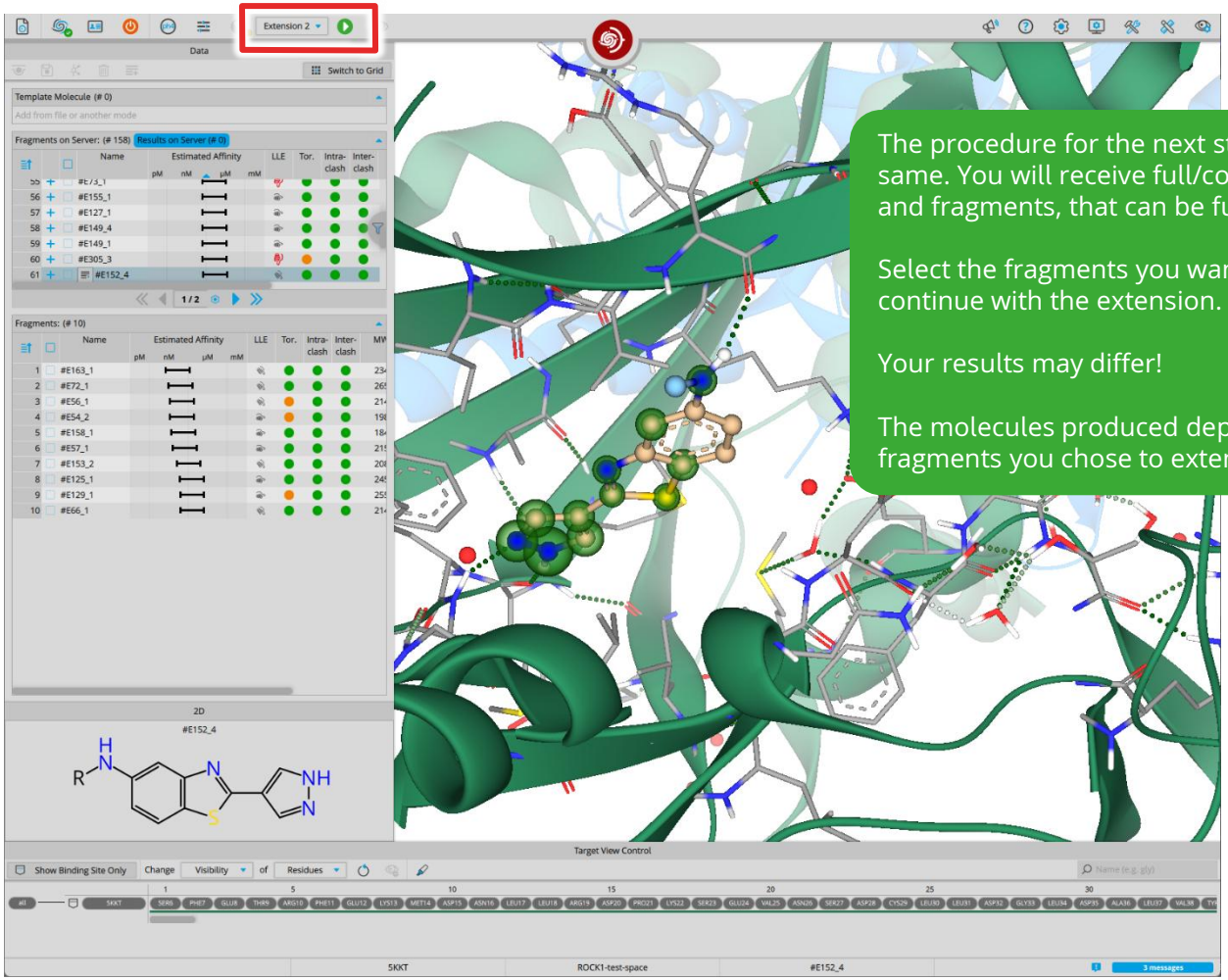
This guide will follow a standard CSD.


Progress bar at top can be used to monitor.
Docking in Progress (16%)
After the run is complete, click on 'View Results' to access Anchoring results.
View Results
Terminate a running workflow.
Anchoring
Docking in Progress (37%)
Please ensure you "Save" the SeeSAR project file after initiating CSD.
Once the run begins, you may close the SeeSAR project and later reopen to monitor the progress or download the results to proceed to next steps.
Important hint
Data
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
5KKT
ROCK1-test-space
No Molecule Selected
2 messages


Torsion and clash filters are applied automatically. The results are sorted based on LE.
Visualize your anchor fragment to the right in 3D. Optionally compare it with respect to your “Template Molecule”.
For this run, 142 poses were generated. Visually assess them for their binding modes. Keep in mind that the light-blue dummy atom is the extension vector for this synthon: All built-up molecules will grow from it.
If it points towards an undesired area (e.g., solvent-exposed lumen or a binding site you do not want to fill), do not pick this pose for the next step.
Important hint
Click “+” to select fragments for the Extension step.
Data
Template or Reference Molecule (# 1)
6U2_A_501
Fragments on Server: (# 113)
Results on Server (# 0)
Name
Estimated Affinity
LLE
#E21_2
#E23_2
#E26_4
#E27_3
#E6_4
#E6_2
2D
#E26_4
R
N
H
N
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
5KKT
ROCK1-test-space
#E26_4
3 messages


Change filters as desired.
Visualization shows feasible extension directions from the linker atom of the fragments in the next step.
Extension 1
Data
Switch to Grid
Template or Reference Molecule (# 1)
6U2_A_501
Fragments on Server: (# 113)
Results on Server (# 0)
Name
Estimated Affinity
LLE
#E17_5
#E15_3
#E29_5
#E7_2
#E29_3
#E13_3
#E16_2
1 / 2
Fragments: (# 4)
#E21_2
#E23_2
#E26_4
#E15_3
2D
#E15_3
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
5KKT
5KKT
ROCK1-test-space
#E15_3
3 messages


After selection of the desired fragments, start the extension step by clicking this button.
Extension 1
Data
Switch to Grid
Template Molecule (# 0)
Add from file or another mode
Fragments on Server: (# 142)
Results on Server (# 0)
Name
Estimated Affinity
LLE
Tor.
Intra-clash
Inter-clash
#E51_5
#E29_1
#E29_3
#E51_5
#E51_3
#E51_1
#E43_2
Fragments: (# 6)
#E48_4
#E30_2
#E49_3
#E45_2
#E51_5
#E43_2
Selected fragments are moved to this table. You can also remove no longer desired fragments to exclude them from the next steps.
2D
#E43_2
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
5KKT
ROCK1-test-space
#E43_2
2 messages

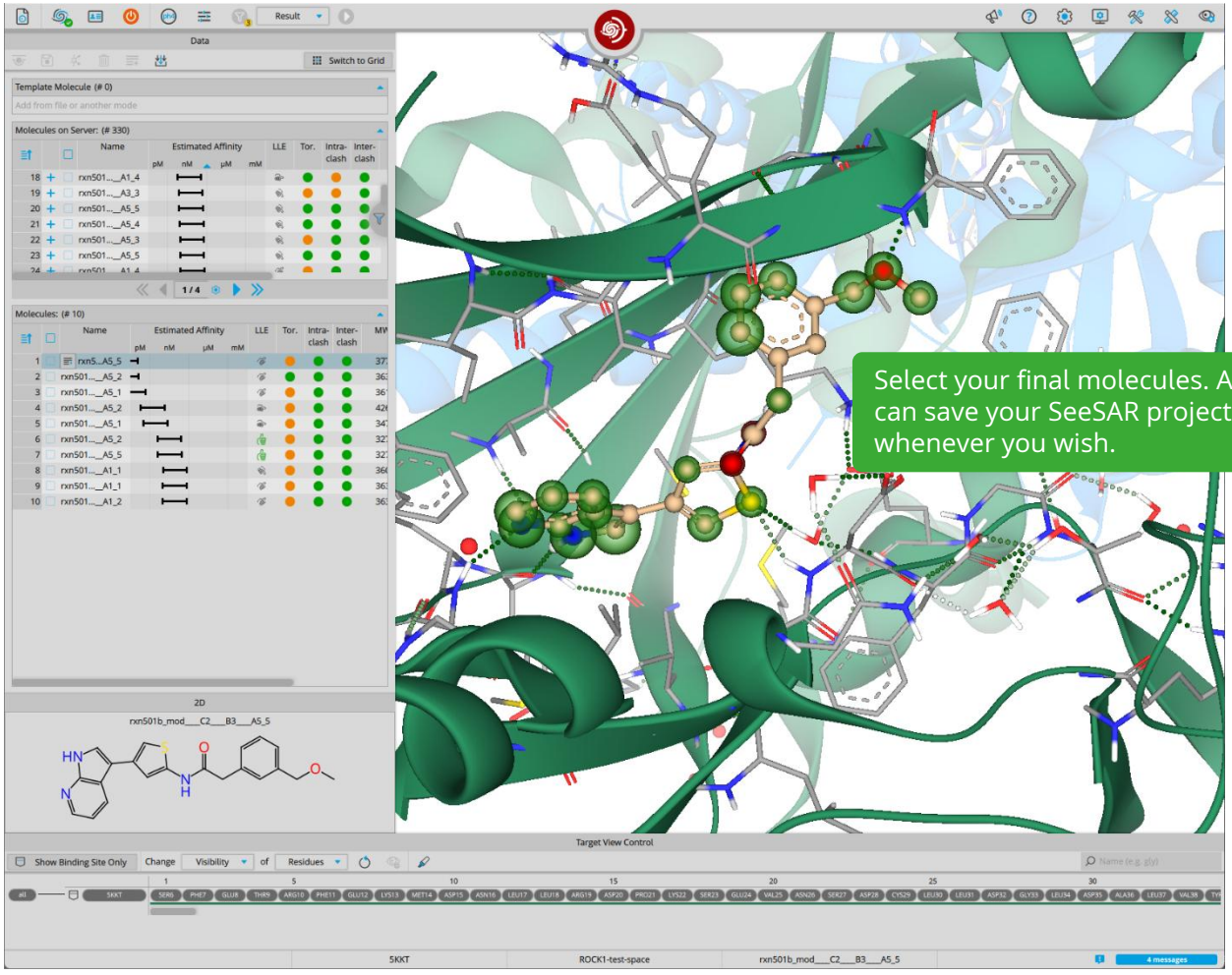


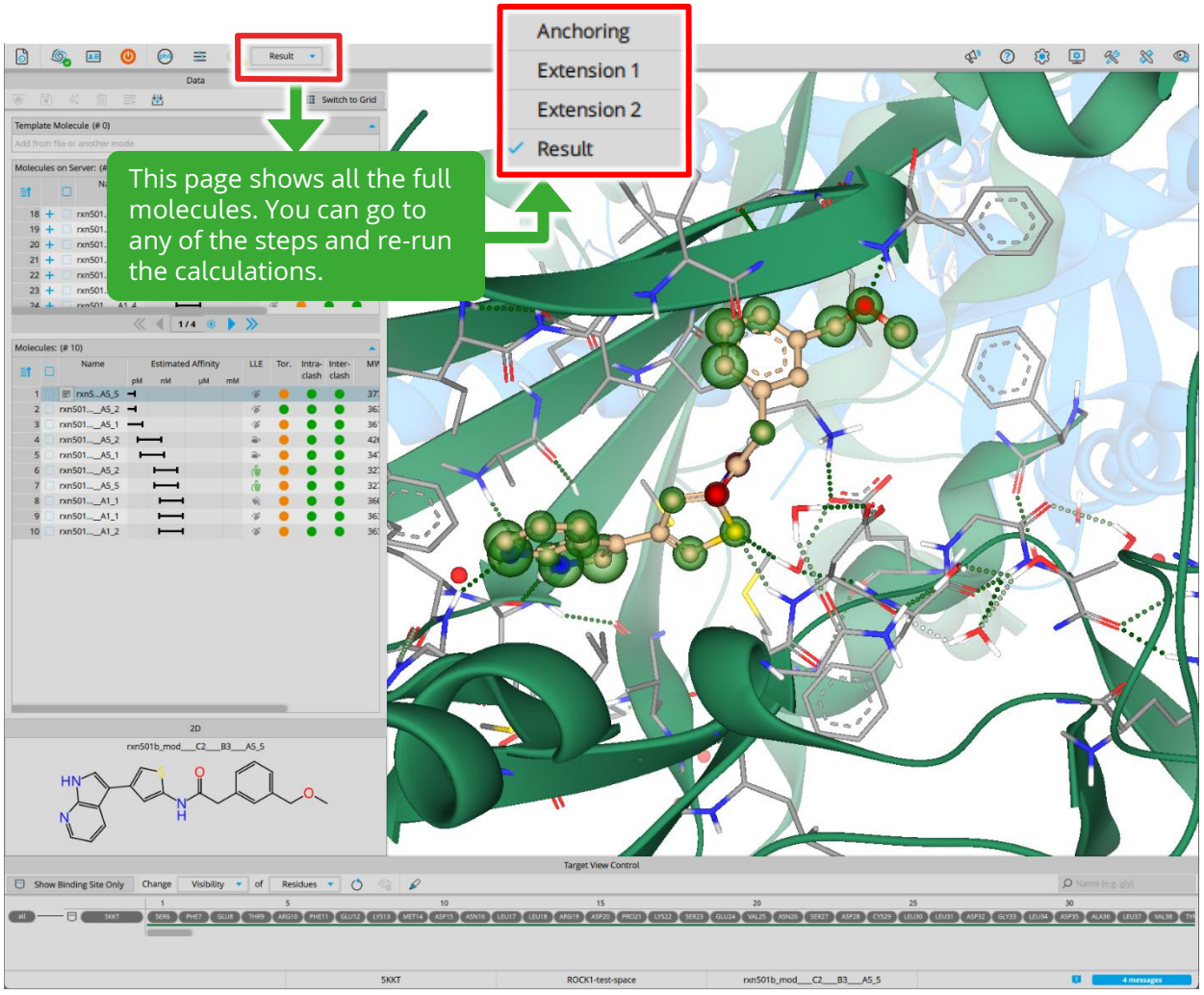
The procedure for the next step remains the same. You will receive full/complete molecules and fragments, that can be further extended.

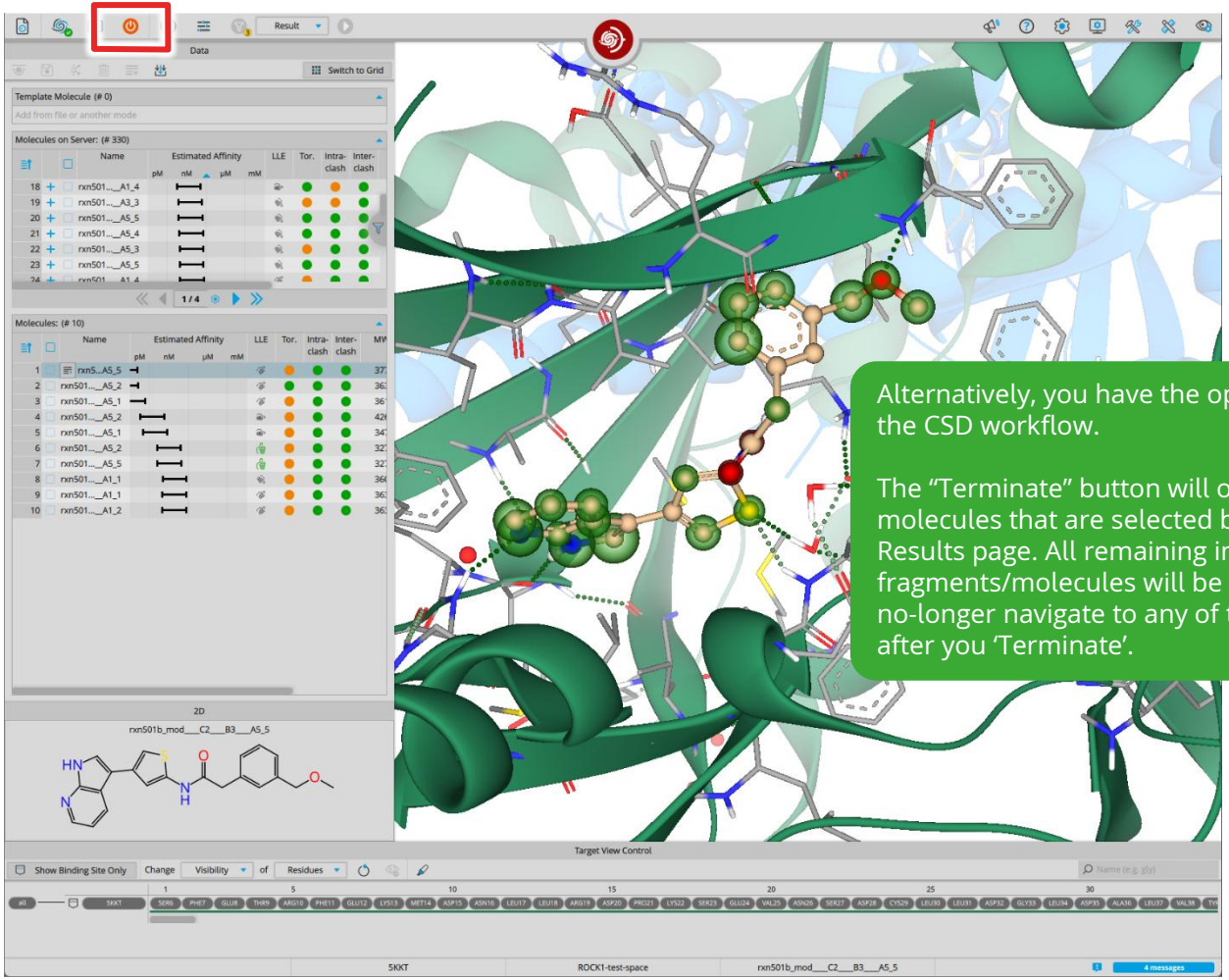
Select the fragments you want to grow and continue with the extension.

Your results may differ!

The molecules produced depend on the fragments you chose to extend.

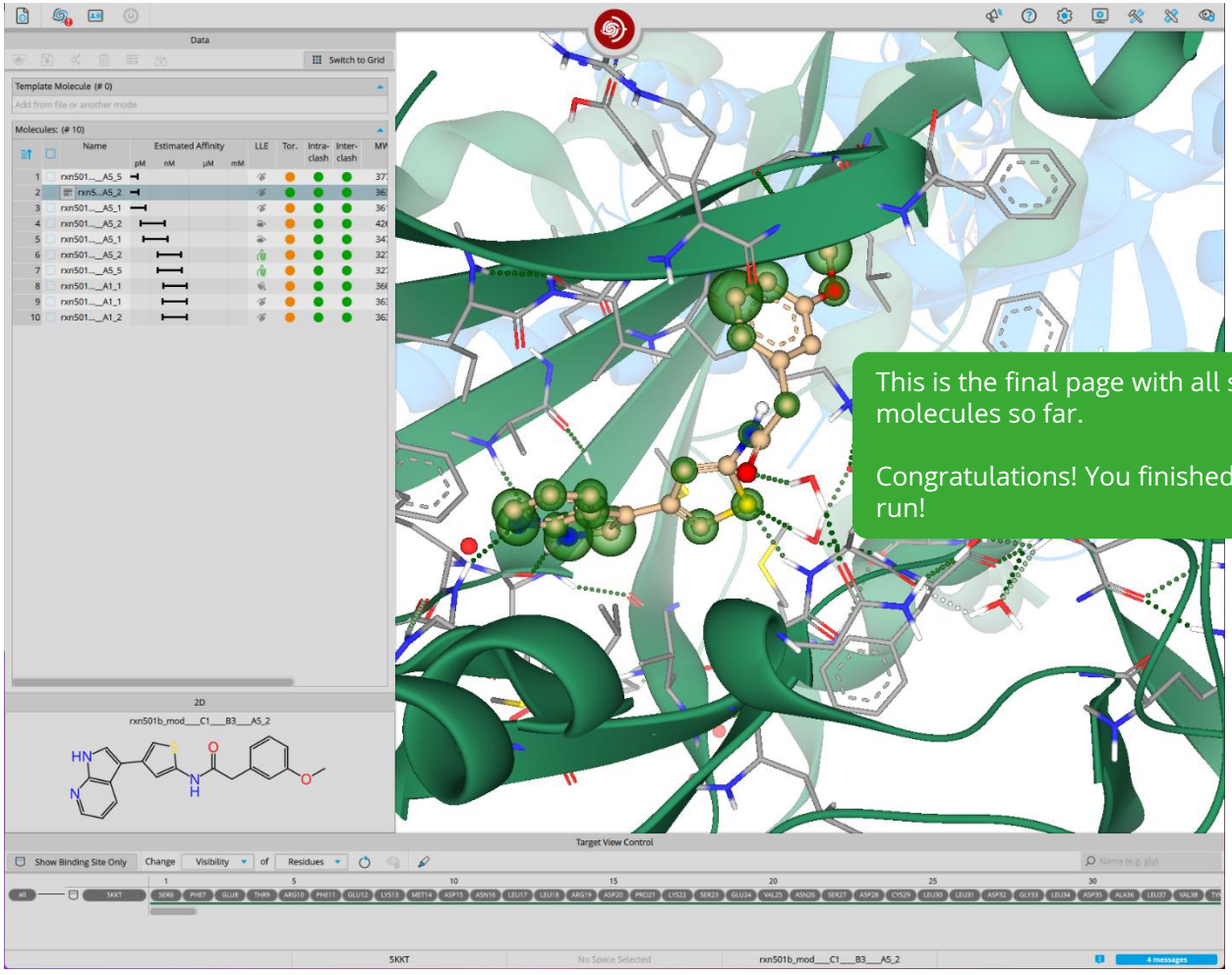

Result
Data
Switch to Grid
Template Molecule (# 0)
Add from file or another mode
Molecules on Server: (# 330)
Name
Estimated Affinity
LLE
Tor.
Intra-clash
Inter-clash
1 / 4
Molecules: (# 10)
2D
rxn501b_mod___C2___B3___A5_5
Select your final molecules. At this stage, you can save your SeeSAR project and return to it whenever you wish.
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
5KKT
ROCK1-test-space
rxn501b_mod___C2___B3___A5_5
4 messages


Anchoring
Extension 1
Extension 2
Result
This page shows all the full molecules. You can go to any of the steps and re-run the calculations.
Result
Data
Switch to Grid
Template Molecule (# 0)
Molecules on Server:
Molecules: (# 10)
Name
Estimated Affinity
LLE
Tor.
Intra-clash
Inter-clash
2D
Target View Control
Show Binding Site Only
Change
Visibility
of
Residues
5KKT
ROCK1-test-space
4 messages



Alternatively, you have the option to 'Terminate' the CSD workflow.

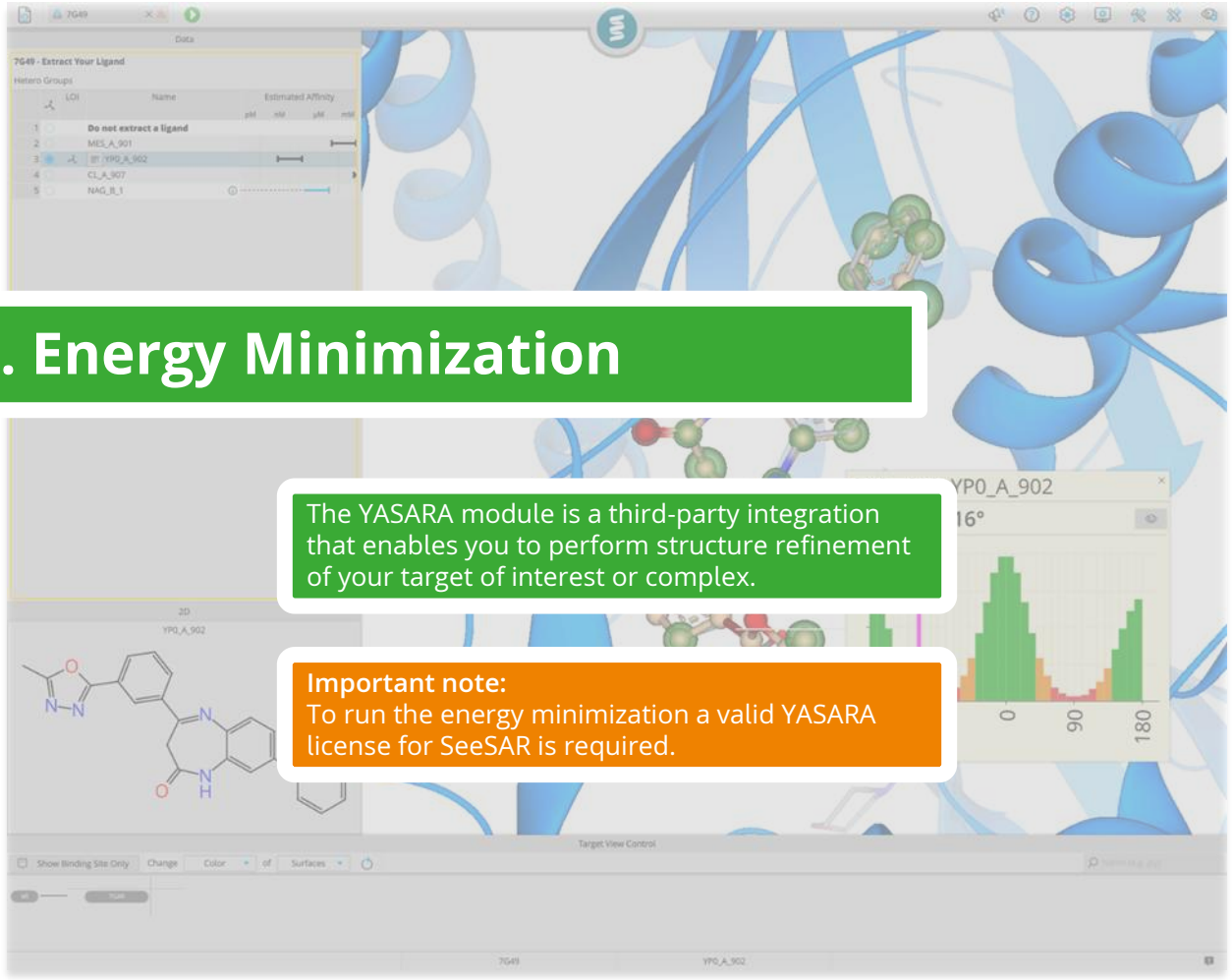
The "Terminate" button will only show the full molecules that are selected below, into a Results page. All remaining intermediate fragments/molecules will be deleted. You can no-longer navigate to any of the previous steps after you 'Terminate'.



This is the final page with all selected full-molecules so far.

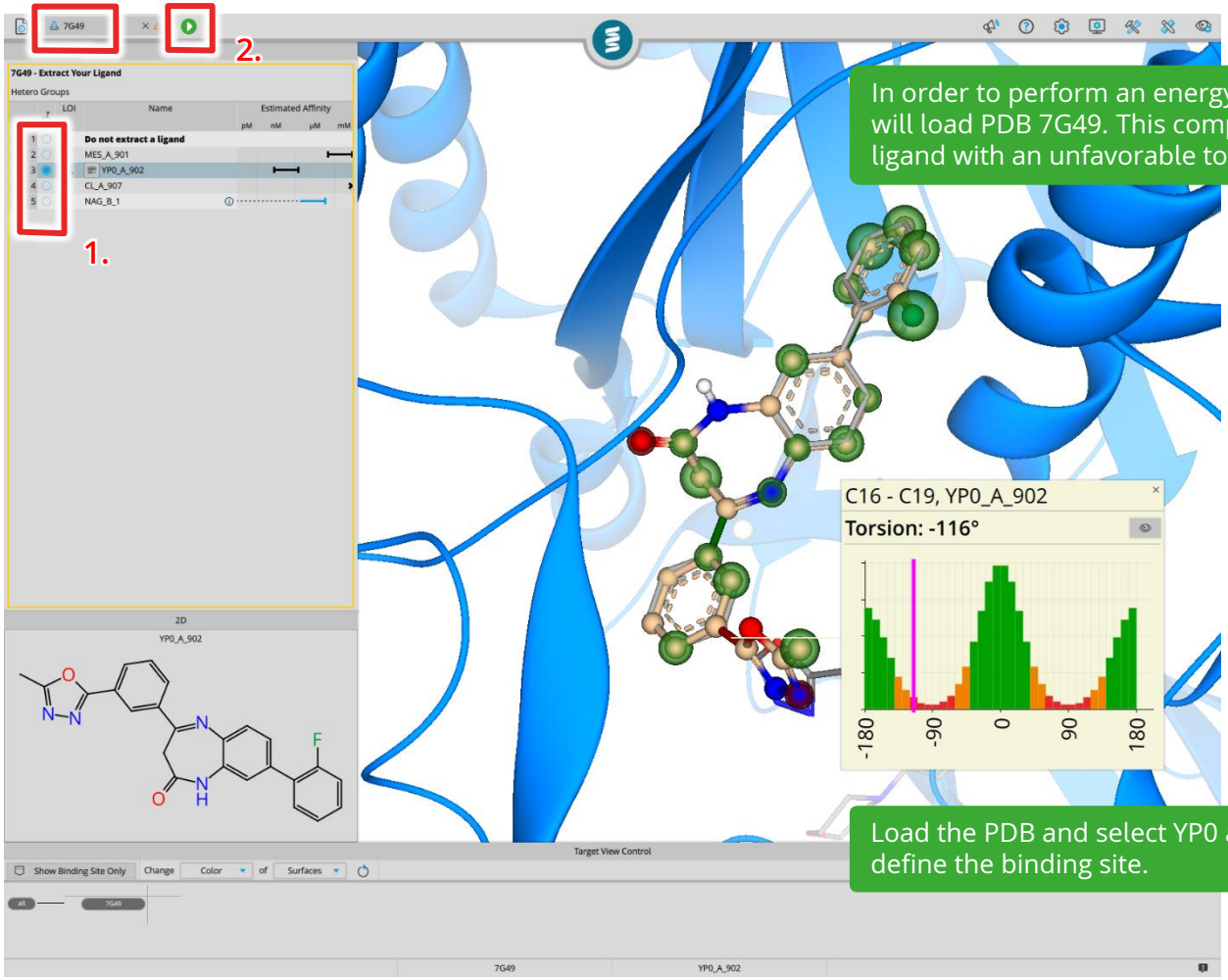
Congratulations! You finished your first C-S-D run!

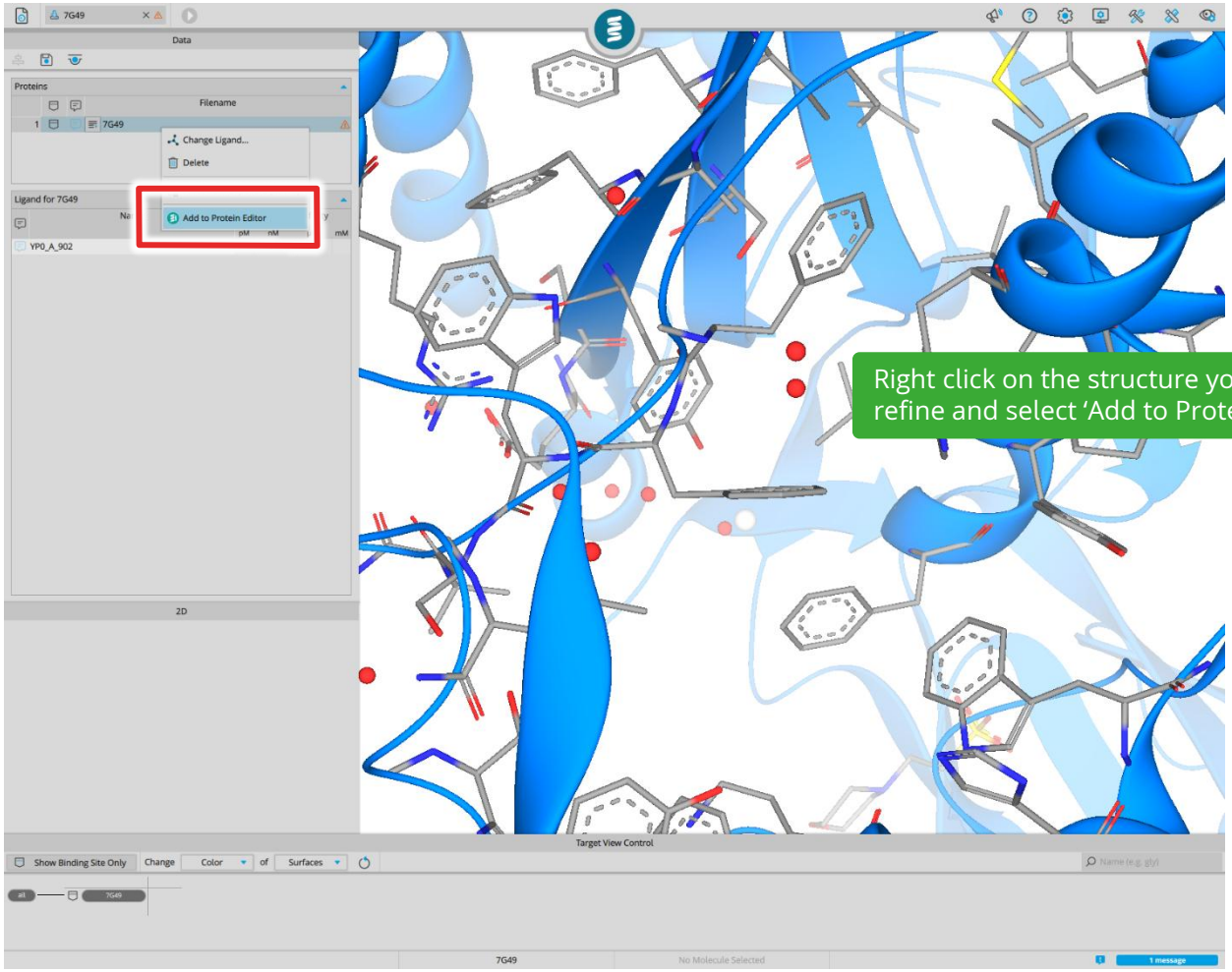
9. Energy Minimization



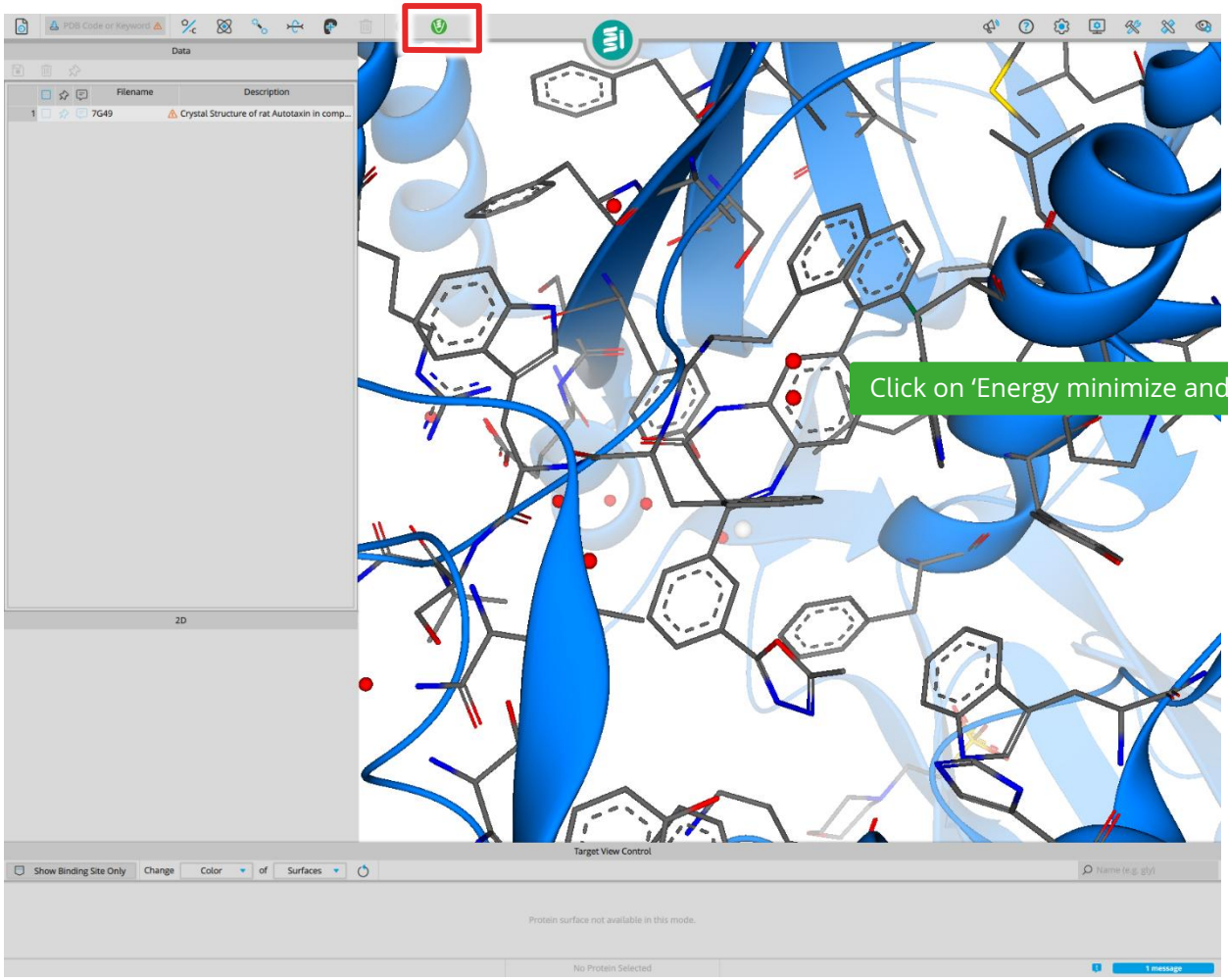
The YASARA module is a third-party integration that enables you to perform structure refinement of your target of interest or complex.

Important note:
To run the energy minimization a valid YASARA license for SeeSAR is required.

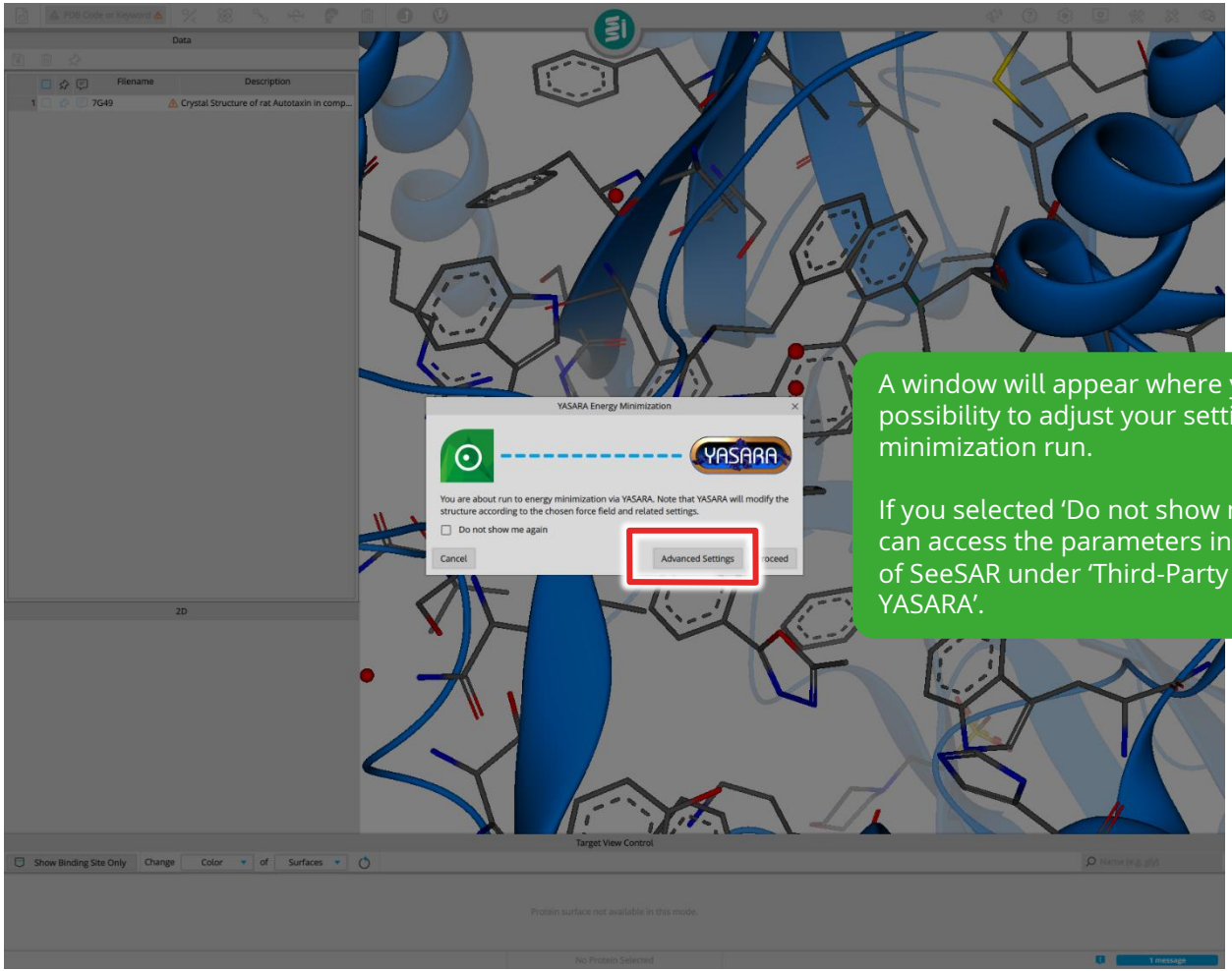

7G49
2.
7G49 - Extract Your Ligand
Hetero Groups
LOI
Name
Estimated Affinity
pM nM µM mM
1 Do not extract a ligand
2 MES_A_901
3 YP0_A_902
4 CL_A_907
5 NAG_B_1
1.
2D
YP0_A_902
C16 - C19, YP0_A_902
Torsion: -116°
-180 -90 0 90 180
In order to perform an energy minimization, we will load PDB 7G49. This complex contains a ligand with an unfavorable torsion.
Load the PDB and select YP0 as the ligand to define the binding site.
Target View Control
Show Binding Site Only
Change
Color
of
Surfaces
7G49
YP0_A_902



Right click on the structure you would like to refine and select ‘Add to Protein Editor’.

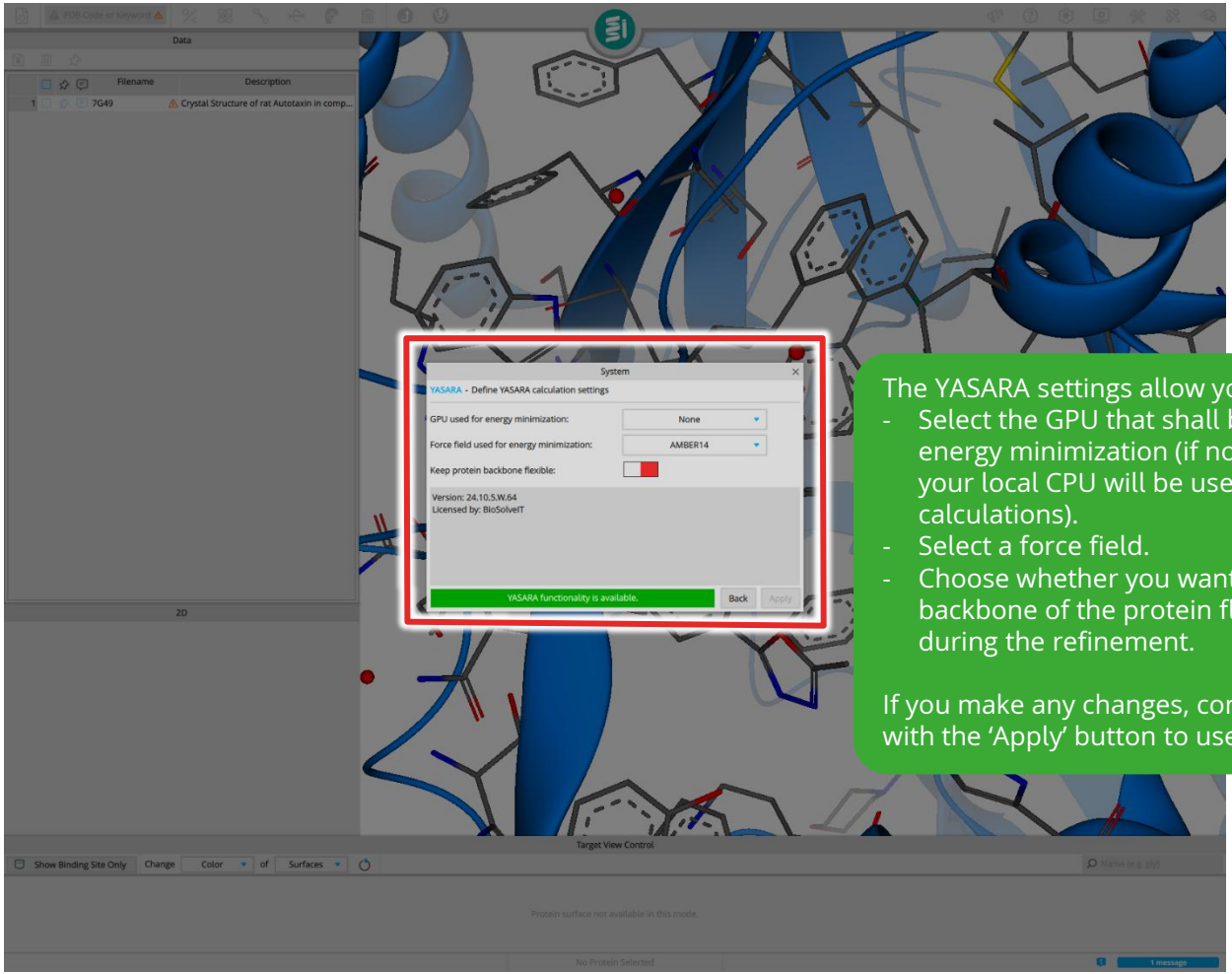


Click on ‘Energy minimize and save to table’.



A window will appear where you will have the possibility to adjust your settings or start the minimization run.

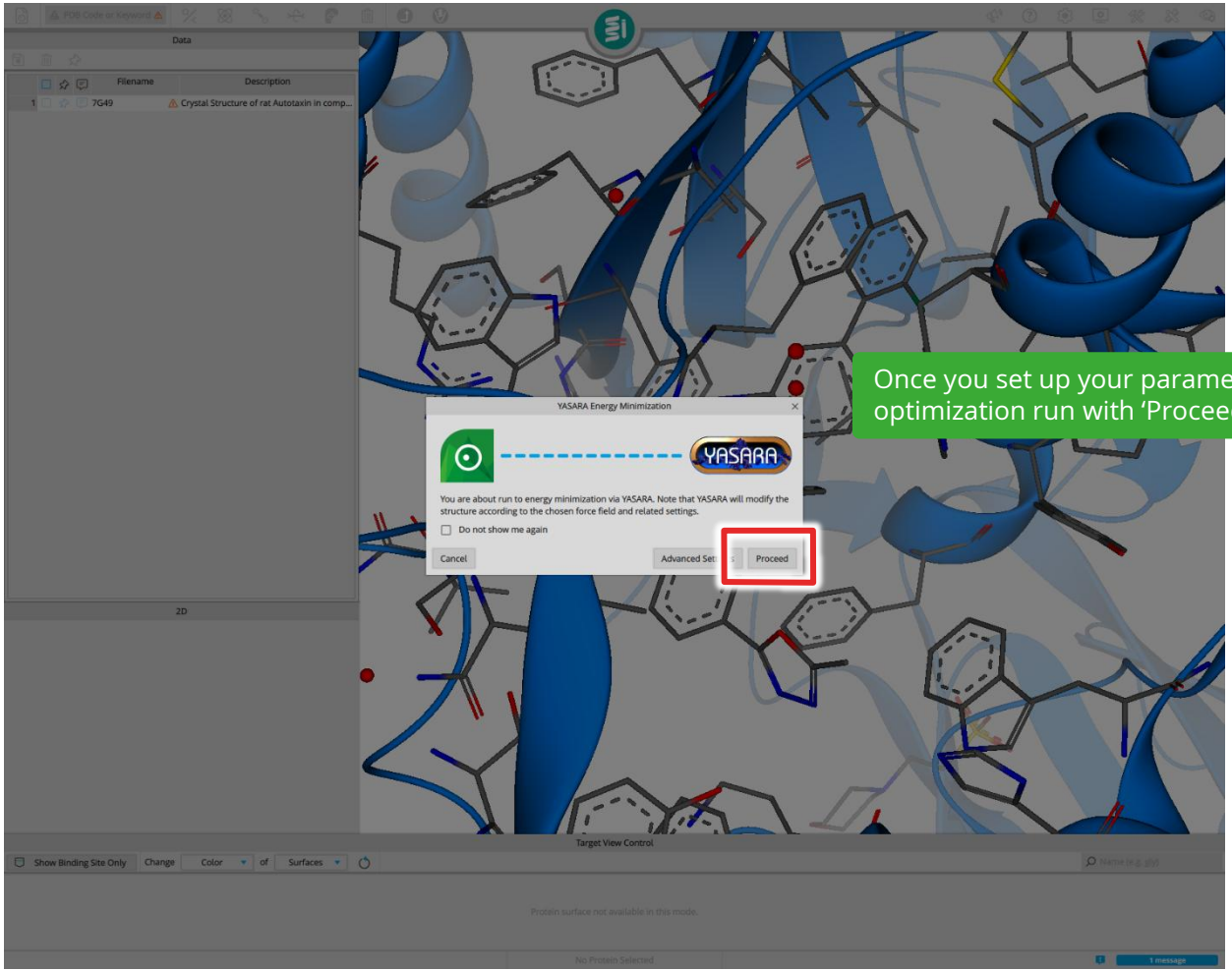
If you selected 'Do not show me again', then you can access the parameters in the 'System' menu of SeeSAR under 'Third-Party Integrations → YASARA'.



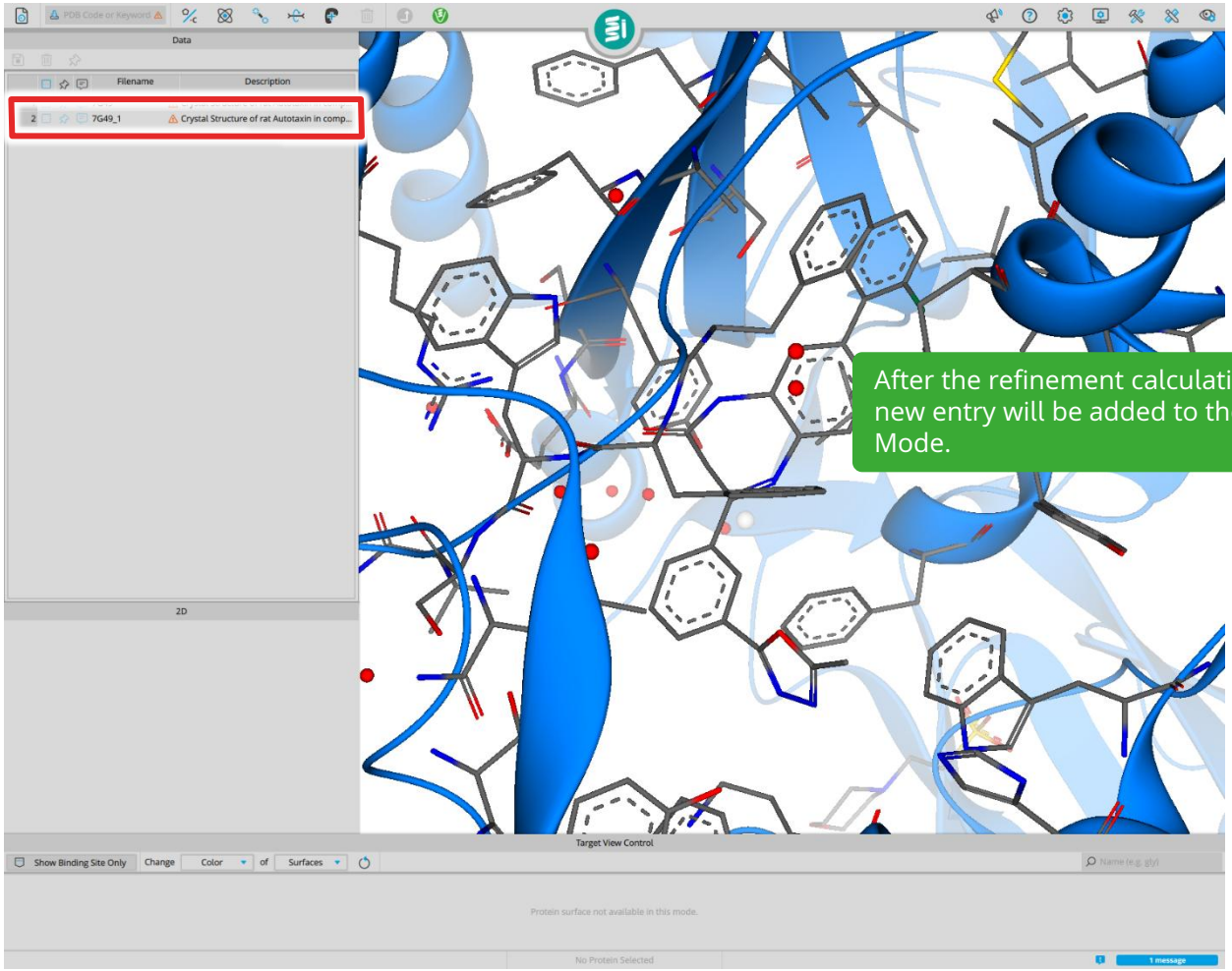
The YASARA settings allow you to:

- Select the GPU that shall be used for the energy minimization (if no GPU is selected, your local CPU will be used for the calculations).
- Select a force field.
- Choose whether you want to keep the backbone of the protein flexible or rigid during the refinement.

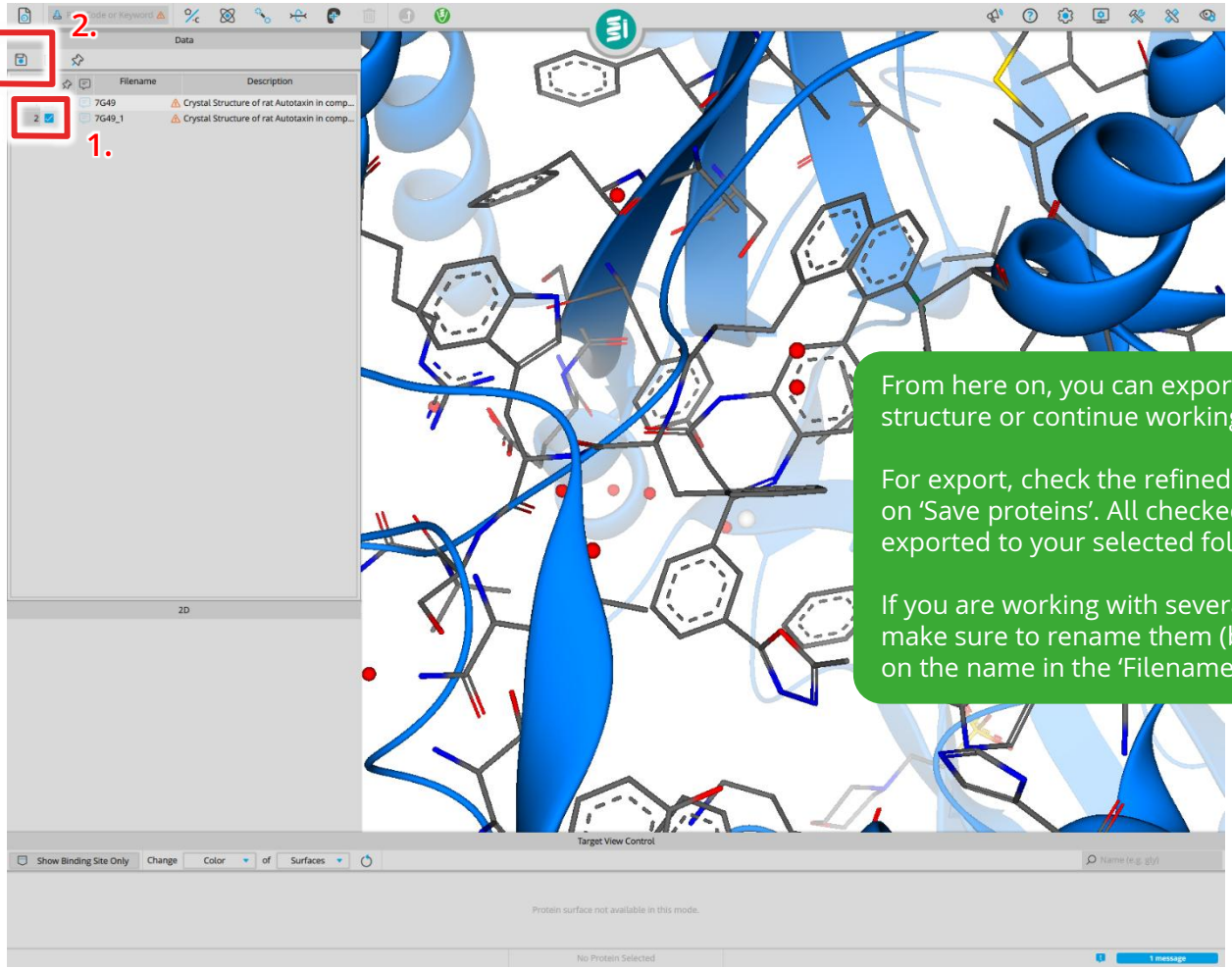
If you make any changes, confirm the settings with the ‘Apply’ button to use them.



Once you set up your parameters, start the optimization run with ‘Proceed’.



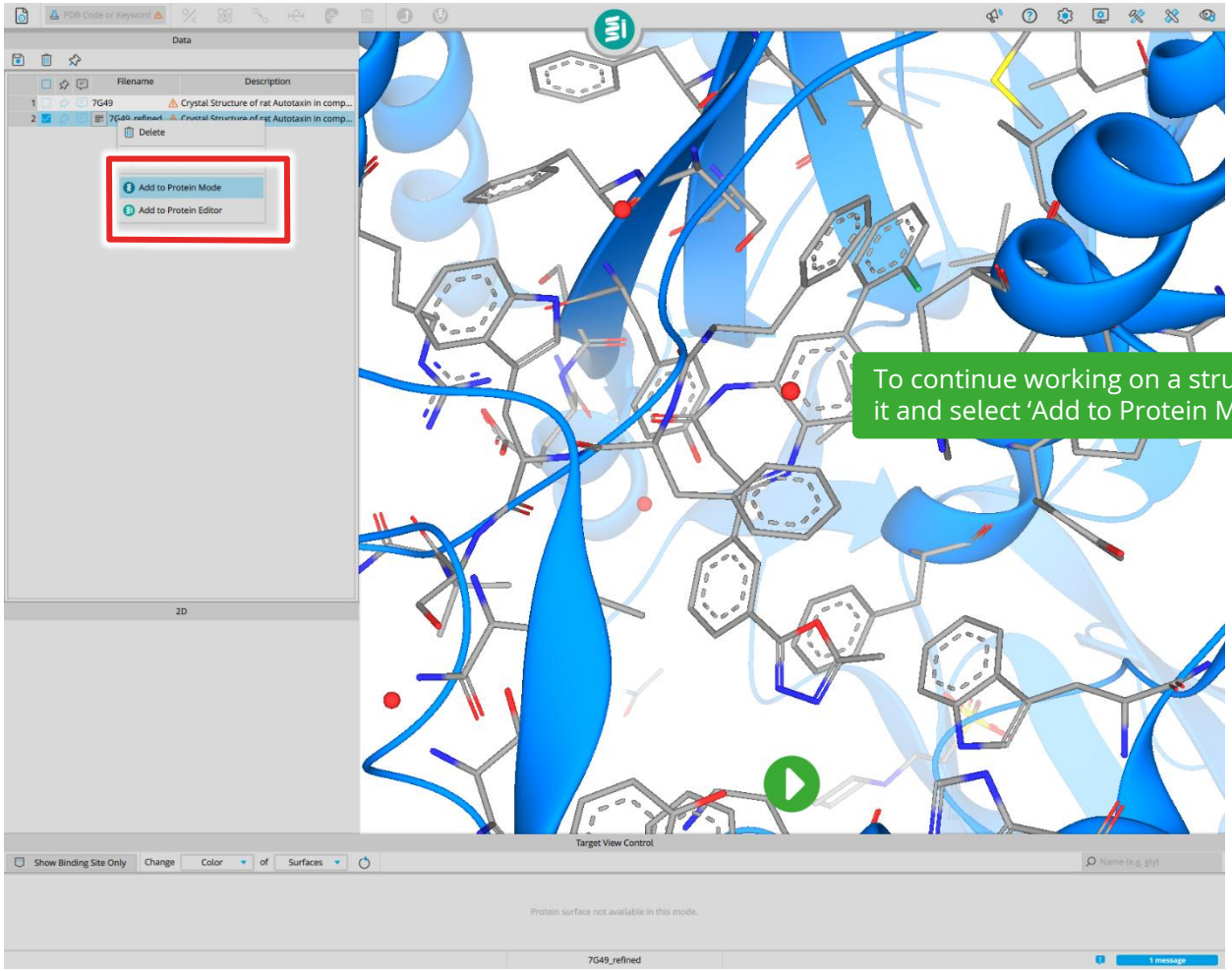
After the refinement calculation has finished, a new entry will be added to the Protein Editor Mode.

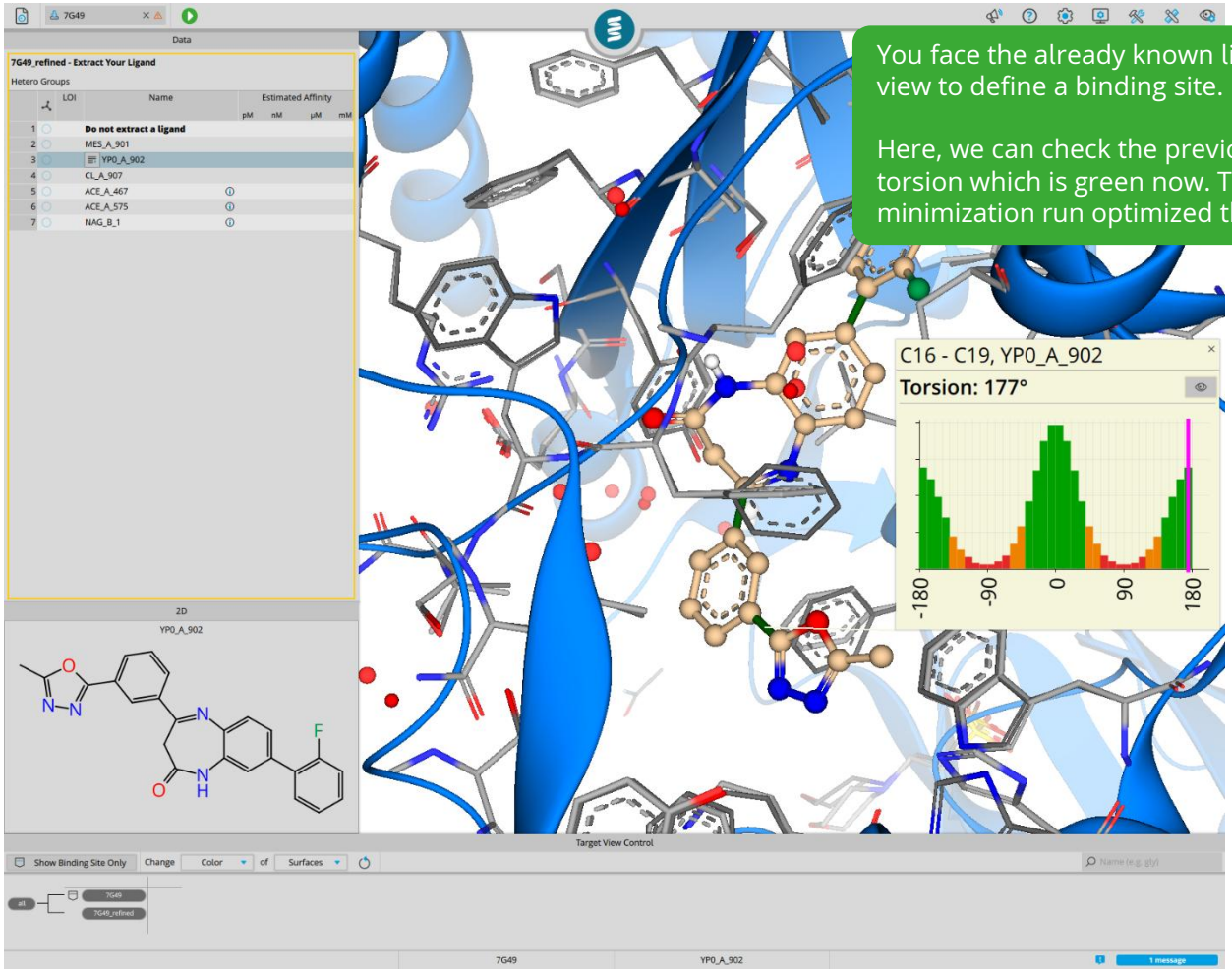


From here on, you can export the refined structure or continue working with it.

For export, check the refined structure and click on ‘Save proteins’. All checked proteins will be exported to your selected folder.

If you are working with several structures, make sure to rename them (by double clicking on the name in the ‘Filename’ column).


Data
Filename
Description
7G49
Crystal Structure of rat Autotaxin in comp...
Delete
Add to Protein Mode
Add to Protein Editor
2D
To continue working on a structure, right click on it and select 'Add to Protein Mode'.
Target View Control
Show Binding Site Only
Change
Color
of
Surfaces
Protein surface not available in this mode.
7G49_refined
1 message



You face the already known ligand selection view to define a binding site.

Here, we can check the previously red colored torsion which is green now. The energy minimization run optimized the strained torsion.

Have fun and enjoy your interactive drug discovery journey with SeeSAR!

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